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A STUDY OF EIGHTY CASES OF EMPYEMA AT CAMP UPTON *

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Even a casual observation of the cases of empyema which have appeared in the Base Hospital at Camp Upton during the past winter and spring shows that we are dealing for the most part with an altogether different type of this disease from that to which we are accustomed. The very early appearance of this complication in the course of pneumonia, its unusual bacteriology and the very high mortality which accompanies it, even under favorable conditions, are the most striking and important variations. Closer study indicates a different train of symptoms, certain alterations in physical signs and a modified pathologic picture; while operative procedures, which, when resorted to in ordinary empyemas give almost uniformly good results, have in this epidemic been attended by so high a death rate as to cause both physician and surgeon to question seriously their advisability, value and type.

In view of these deviations from the usual in this frequent cantonment infection, a close study of all cases was imperative. In this problem it was at once apparent that closely associated laboratory and clinical methods must be constantly applied, and a large portion of the work of the medical and laboratory staffs of this hospital has been devoted during the past winter, to this insistent problem. This study has been a conjoint clinical and laboratory one, far more than is usually the case, for it has been found absolutely necessary that the laboratory staff follow the clinical aspects of the cases, even to the point of studying the physical signs, and a proper clinical comprehension of the individual case has been found inseparably connected with the work in the laboratory.

Analysis of the clinical picture and the laboratory findings soon showed us that we were dealing with a specific and virulent infection

* Submitted for publication May 18, 1918.

TABLE 1.—Data of Empyema Cases

No	Type of Pneumonia	Onset of Empyema	Type of Organism		Blood Culture	Treatment	Termination	Post Mortem Findings
			Sputum	Pleural				
1	Sec. infl.	4/10-4/16	Pn. II	Pn. II	.....	Aspiration	Died 4/17/18	
2	Primary	1/ 9-1/14	Pn. I	Pn. I	.....	Resection	Recovering	
3	Sec. infl.	12/15-1/ 1	Pn. I	Pn. I	.....	Resection		
4	Sec. infl.	12/18-1/ 4	Pn. I	Pn. I	Neg.	Resection	Duty 2/19/18	
5	Sec. pleur.	3/15-3/22	Pn. II	Pn. II	.....	Resection	Convalescent	
6	Primary	3/22	Pn. II	Pn. II	.....	No record	Died 3/26/18	Lobar pn., L. U. and L. R. U., emp. lt.
7	.....	2/ 1-2/22	Pn. II	Pn. II	Pn. II	Thoracotomy	Duty	
8	Sec. infl.	3/ 7-4/ 8	Pn. IV	Pn. IV	.....	Resection	Prognosis (?)	
9	Primary	3/26-3/30	Pn. IV	Pn. IV	.....	No record	Died 4/3/18	Lobar pn., rt. bilat., emp. sacc.
10	Sec. mitral stenosis	1/4	Pn. IV	Pn. IV	Pn. IV	No record	Died 1/10/18	Lobar pn., L. L. L. and Rt. U., emp. lt., veg. endocarditis, infarcts in lt. lung
11	Sec. infl.	12/25-1/ 1	Pn. IV	Pn. IV	.....	No record	Duty 1/3/118	
12	Sec. bron.	3/18-4/ 2	Pn. IV	Pn. IV	.....	Resection	Prognosis (?)	
13	Primary	3/12-4/ 6	Pn. IV	Pn. IV	.....	Resection	Prognosis (?)	
14	Primary	.....	Pn. II	Pn. IV	.....	Resection	Convalescent	
15	Primary	4/ 6-4/14	Pn. IV	Pn. IV	.....	Aspiration	Died 4/14/18	
16	Primary	2/ 7-2/21	Strep. haem.	Strep. haem.	Neg.	Resection		
17	Primary	3/12-3/13	Strep. haem.	Strep. haem.	Neg.	Resection	Died 3/23/18	Bronchopn., emp. sacc. rt., abscesses in rt. lung. fibrinopur. pericarditis
18	Primary	3/18-3/30	Strep. haem.	Strep. haem.	Neg.	Resection	Convalescent	
19	Primary	3/ 3-4/ 4	Strep. haem.	Strep. haem.	.....	Aspiration	Died 4/12/18	Bronchonpn., emp. rt. sacc.
20	Primary	3/13-4/ 3	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	
21	Primary	3/30-4/ 1	Strep. haem.	Strep. haem.	.....	Aspiration	Died 4/2/18	Bronchopn., emp lt. L. L. L., acute fibrino. pericarditis
22	Primary	3/12-3/21	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	
23	Sec. bron.	3/25-3/31	Strep. haem.	Strep. haem.	.....	Resection	Prognosis (?)	
24	Primary	4/ 5-4/ 9	Strep. haem.	Strep. haem.	.....	Aspiration	Died 4/10/18	Bronchopn., lt. emp. lt. f., fibrinous pericarditis
25	Primary	3/29-4/ 2	Strep. haem.	Strep. haem.	Neg.	No record	Died 4/3/18	Bronchopn., (interst.) emp. lt.
26	Sec. bron.	3/ 9-3/20	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	

27	Primary	3/21–4/ 9	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	
28	Sec. measles	3/26–4/ 3	Strep. haem.	Strep. haem.	.....	Aspiration	Died 4/11/18	Lob. pn. rt. lobe, emp. rt. sacc., emp. lt.
29	Sec. bron.	3/16–3/17	Strep. haem.	Strep. haem.	.....	Resection	Died 3/18/18	
30	Sec. bron., pharyngitis, G. measles	1/ 7–1/17	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	
31	Primary	3/ 4–3/ 5	Strep. haem.	Strep. haem.	.....	Resection	Died 3/5/18	Lobar pn. left lung, emp. lt., central pn. rt. lung
32	Sec. infl.	3/ 5–3/ 9	Strep. haem.	Strep. haem.	.....	Resection	Died 3/10/18	
33	Sec. measles	3/24–4/ 7	Strep. haem.	Strep. haem.	.....	Resection	Convalescent	
34	Primary	3/6	Strep. haem.	Strep. haem.	.....	No record	Died 3/8/18	Lobar pn. L. L. L., emp. lt., mult. abscesses of lung
35	Primary	12/25–1/ 6	Strep. haem.	Strep. haem.	.....	Aspiration	Died 1/17/18	Bronchopn. lt. (interst.) emp. lt., fibrinopur. pericarditis
36	Primary	3/ 1–3/ 3	Strep. haem.	Strep. haem.	.....	Resection	Died 3/3/18	Lobar pn. R. L. L. abscess of lung, emp. rt.
37	Primary	3/11–3/15	Strep. haem.	Strep. haem.	.....	Resection	Died 3/19/18	
38	Primary	2/18–2/20	Strep. haem.	Strep. haem.	Neg.	Resection	Died 3/27/18	Lobar pn. L. L. L., emp. lt., pneumothorax lt. infarcts of spleen
39	Sec. infl.	3/ 7–3/10	Strep. haem.	Strep. haem.	Strep. haem.	Resection	Convalescent	
40	Sec. mumps	2/11–2/23	Strep. haem.	Strep. haem.	Neg.	Resection	Convalescent	
41	Sec. infl.	1/28–2/11	Strep. haem.	Strep. haem.	Neg.	Resection	Died 2/24/18	Bronchopn. R. L. L., lobar pn., L. U. L., emp. rt.
42	Sec. infl.	3/ 5–3/ 5	Strep. haem. (?)	Strep. haem.	.....	Resection	Died 3/11/18	
43	Primary	2/ 4–2/ 9	Strep. haem. (?)	Strep. haem.	.....	Resection	Died 3/12/18	Brochopn. rt. lung (interst.) type, fibrinopur. pericarditis, emp. rt.
44	Sec. mumps	3/ 7–3/ 7	Strep. haem. (?)	Strep. haem.	.....	Resection	Died 3/9/18	Lobar pn. R. L. L., emp. rt. sacc., fibrinopur. pericarditis
45	Primary	2/ 8–3/ 8	Strep. haem. (?)	Strep. haem.	.....	Resection	Died 3/10/18	Bronchopn. bilat., emp. bilat. sacc.
46	Sec. pharyn.	.....	Strep. haem. (?)	Strep. haem.	.....	.....	Died	Sarcoma testes and lung, bronchopn., emp. lt., acute general peritonitis
47	Primary	4/14–4/16	Strep. haem.	Strep. haem.	.....	Aspiration		
48	Sec. tonsil	4/ 5–4/ 6	Strep. haem. (?)	Strep. haem.	.....	.....	Died	Bronchopn. bilat., emp. lt. sacc., fibrinopericarditis
49	Primary	4/17–4/20	Strep. haem.	Strep. haem.	Neg.	Aspiration	Died 4/21/18	
50	Primary	4/17–4/21	Strep. haem. (?)	Strep. haem.	.....	No record		
51	.....	.....	.....	.....	.....	Resection	Convalescent	
52	Primary	1/ 1–1/20	Strep. virid.	Strep. virid.	.....	Incision	Duty	
53	Primary	3/15	Strep. virid.	Strep. virid.	Strep. virid.	No record	Died 3/30/18	Bronchopn. rt. lung, lobar pn. L. L. L., emp. lt. sacc., acute strep. meningitis
54	Primary	1/ 8–1/ 4	Strep. virid.	Strep. virid.	.....	No record	Died 1/14/18	Bronchopn. (interst.) rt. L. L., emp. rt. sacc., fibrinopur. pericarditis
55	Primary	1/12–1/24	Strep. virid.	Strep. virid.	Neg.	No record	Died 2/3/18	Bronchopn. (interst), emp. rt. sacc., fibrinopur. pericarditis

TABLE 1.—DATA OF EMPYEMA CASES—*Continued*

No.	Type of Pneumonia	Onset of Empyema	Type of Organism		Blood Culture	Treatment	Termination	Post Mortem Findings
			Sputum	Pleural				
56	Primary	12/15	Pn. II	Strep. virid.	.....	No record	Died 12/29/17	Bronchopn. and lobar pn. (bilat. interst.), emp. lt., mult. abscesses of lungs
57	Sec. infl.	.....	Pn. II	Strep. haem.	.....	No record	Died 2/11/18	
58	Sec. infl.	1/ 3-2/14	Pn. II	Strep. haem.	.....	Resection	Prognosis (?)	
59	Sec. tonsil., bronch. (?)	1/21-2/17	Pn. III	Strep. haem.	.....	Resection	Recovering	
60	Sec. infl., pharyn.	1/18-1/26	Pn. IV	Strep. haem.	.....	Resection	Died 1/28/18	
61	Primary	12/22-1/20	Pn. IV	Staph. aures.	Neg.	Resection	Died 2/11/18	
62	Sec. bron.	12/21-12/29	Pn. IV	Strep. virid.	.....	No record	Died 12/21/17	Bronchopn. and lobar pn. (interst.), emp. sacc. rt., fibrinopur. pericarditis, mult. abscesses of rt. lung
63	Primary	1/22-2/18	Pn. IV	Strep. haem.	Neg.	Resection	Convalescent	
64	Primary	3/4	Pn. IV	Strep. haem.	Neg.	Resection	Died 3/13/18	Lobar pn. lt. lung and rt. L. L., emp. rt.
65	Sec. mumps	1/26-2/19	Pn. IV	Strep. haem.	.....	Resection	Convalescent	
66	Sec. measles	12/6-1/27	Pn. I	Sterile	.....	Resection	Convalescent	
67	Sec. infl.	3/27-3/30	Pn. I	Sterile	.....	Aspiration	Died 4/1/18	
68	Sec. pleurisy	2/ 6-2/20	Pn. II	Sterile	Neg.	Resection	Died 3/15/18	
69	Primary	2/26	Pn. II	Sterile	Neg.	No record	Died 3/3/18	
70	Sec. measles	12/18-1/ 3	Pn. III	Sterile	Neg.	Resection	Died 3/5/18	General miliary T.B., lobar pn. lt. lung, emp. lt.
71	Primary	1/30-2/25	Pn. IV	Sterile	.....	No record	Duty 4/7/18	
72	Primary	3/30-4/ 9	Pn. IV	Sterile	.....	No record		
73	Primary	1/ 3-1/25	Pn. IV	Sterile	.....	Resection	Died 1/21/18	
74	Sec. bron.	3/ 7-3/11	Pn. IV	Sterile	.....	Aspiration	Duty	
75	Primary	3/21-3/23	Pn. IV	Sterile	.....	Aspiration	Convalescent	
76	Sec. bron.	3/11	Strep. haem.	Sterile	.....	No record	Died 4/19/18	
77	Primary	4/ 8-4/15	Strep. haem.	Sterile	.....	No record	Convalescent	
78	Sec. scarlet	3/30	Strep. haem.	Sterile	.....	No record		
79	Sec. bron.	1/ 7-1/14	Strep. virid.	Sterile	.....	Resection	Died 3/3/18	
80	Sec. infl.	3/12-3/17	Strep. virid.	Sterile	Neg.	Resection	Duty 4/22/18	

by an organism which is rarely encountered in civil infections of the lung and pleura. In most of these cases the organism in question — the so-called *Streptococcus haemolyticus* — has been the causative agent, not only of the empyema, but of the pneumonia associated with it. The relation between streptococcus pneumonia and the incidence of empyema is well shown by a comparison of the different types of pneumonia which have been encountered at Camp Upton.

During the period from Oct. 7, 1917, to April 20, 1918, 300 cases of pneumonia were admitted to the Base Hospital at Camp Upton. Of the 300 pneumonias, 283 had careful bacteriologic examinations of the sputum; 136, or almost half, were found to be of streptococcus origin, and 137 were caused by the pneumococcus. There were 49 cases of streptococcus empyema, showing an incidence of empyema among the streptococcus pneumonias of 36 per cent. On the other hand, there were only 15 cases of pneumococcus empyema, or an incidence of empyema among the pneumococcus cases of 11 per cent. Finally, there were 15 cases of sterile empyema about equally divided between streptococcus and pneumococcus pneumonia. Altogether, our records show for this period, 80 cases of empyema, and these 80 cases form the basis for this study.

Before proceding to the discussion of empyema proper it might be well to refer briefly to the relation of measles to this disease. In some of the other camps a large percentage of the empyemas, especially those of streptococcus origin, have developed as a complication of post-measles pneumonia. Such has not been the case at Camp Upton. In the first place, a comparatively small number of our measles patients have developed pneumonia — thirty out of 164 cases, with a mortality list of but two. Furthermore, only four cases of empyema (Cases 28, 33, 66 and 70) have developed among these thirty pneumonias, and of these only two patients died. By referring to Table 1, however, it will be seen that a considerable number of the empyemas developed in pneumonias which followed influenza, tonsillitis and other mild infections. We are quite certain, however, that streptococcus empyema may develop from a primary streptococcus pneumonia. Two of the pneumonia cases which followed mumps (Cases 40 and 44) were complicated by empyema, both of these being streptococcus infections.

In this study special attention has been devoted to the bacteriologic examination of the cases. In most instances direct specimens of the patients' pleural exudate were collected as soon as the diagnosis was made, and taken to the laboratory at once for examination. The bacteriology of the sputum was carried out as follows: A fresh specimen of sputum was thoroughly washed with sterile saline and smears made for the gram stain. The sputum was then emulsified and 0.5 c.c. added to a tube of Avery's blood broth, which was incubated in the

water bath at 37 C. for five hours. At the end of this time smears were made and if a pure culture was found agglutination tests were made at once in the usual manner. Under all conditions, however, subcultures were made from broth or plain agar plates and colonies were picked from these on the following day for further study. In many cases the blood broth method was controlled by injections of the sputum into the mouse and identification of the organism was determined from the peritoneal exudate or the heart's blood. In a few instances cultures of the sputum were made directly on blood agar plates. The results obtained by the various methods have been surprisingly consistent.

TABLE 2.—CLASSIFICATION OF EIGHTY EMPYEMAS

	Cases	Deaths
I. Pneumococcus in both sputum and pleural exudate:		
Type I in both	3	0
Type II in both	4	2
Type IV in both	6	2
Type II in sputum; Type IV in pleural exudate	1	0
Sputum not examined; Type IV in pleural exudate	1 (?)	1
	15	5 (33%)
II. Streptococcus in both sputum and pleural exudate:		
Strept. hemol. in both	29	16
Sputum not examined; strept. hemol. in pleural exudate	7 (?)	6
Strept. virid. in both	4	3
	40	25 (60%)
III. Mixed infections:		
Pn. Type II in sputum; strept. vir. in pleural exudate	1	1
Pn. Type II in sputum; strept. haem. in plural exudate	2	1
Pn. Type III in sputum; strept. haem. in pleural exudate	1	0
Pn. Type IV in sputum; strept. haem. in pleural exudate	4	2
Pn. Type IV in sputum; strept. vir. in pleural exudate	1	1
Pn. Type IV in sputum; staph. aur. in pleural exudate	1	1
	10	6 (60%)
IV. Sterile empyemas:		
Pn. Type I sputum	2	1
Pn. Type II sputum	2	2
Pn. Type III sputum	1	1
Pn. Type IV sputum	5	1
Streptococcus haemolyticus	3	1
Streptococcus viridans	2	1
	15	7 (50%)

CLASSIFICATION OF EMPYEMAS

By referring to Table 2 it will be seen that our eighty cases of empyema naturally fall into three groups: (1) pneumococcus empyemas; (2) streptococcus empyemas; (3) sterile empyemas. These three groups will be discussed separately.

1. *Pneumococcus Empyemas.*—In the present series of eighty cases there were only fifteen that showed the pneumococcus from culture of the pleural exudate. These pneumococcus empyemas differed in no essential respect from those seen in civil practice. Without exception

they developed in cases of lobar pneumonia in which the pneumococcus had been previously isolated from the sputum. This type of empyema usually comes on late in the course of the disease when the patient is convalescent. There is a sudden rise in temperature and a corresponding increase in pulse rate. The patient, however, may not be very ill. Frank signs of fluid are usually present and on exploring the chest over this area cloudy or creamy pus is withdrawn which on examination shows many pus cells and capsulated pneumococci.

Pneumococci of Types I, II and IV are all represented in this group, and in all except one case the same kind of pneumococcus was found in both sputum and pleural exudate. In this case (Case 14) pneumococcus Type II, atypical, was isolated from the sputum, and pneumococcus Type IV from the pleural fluid. Of this group of fifteen cases, five patients died, a mortality of 33 per cent. One patient (Case 10) developed a pneumococcus endocarditis and septicemia. One of the Type II cases (Case 7) on blood culture showed twenty-four colonies per cubic centimeter of blood, but the patient made an excellent recovery after rib resection and drainage. This patient showed a curious metastatic focus, a perithyroid abscess. In the fatal cases of this group the men all died early in the disease apparently from the intensity and extent of the pneumonia rather than from the concomitant empyema.

2. *Streptococcus Empyemas.*—By far the largest number of our empyema cases were streptococcus infections, and it is this group that constitutes the most interesting phase of the problem. For convenience of discussion it will be well to divide this group into three subgroups.

(*a*). *Streptococcus haemolyticus* empyema.

(*b*). *Streptococcus viridans* empyemas.

(*c*). Streptococcus empyemas following pneumococcus pneumonia.

(*a*). *Streptococcus Haemolyticus Empyemas*: In this group there were twenty-nine cases in which *Streptococcus haemolyticus* was recovered in pure culture from the empyema fluid and in which bacteriologic examination of the sputum showed the same organism. There were seven other cases in which the hemolytic streptococcus was recovered from the pleural exudate, but in which for some unavoidable reason the sputum was not examined. In these seven cases, however, the clinical course and physical signs strongly indicated a streptococcus pneumonia, so they probably belong to this group. These thirty-six cases constitute a fairly definite and characteristic picture. The patient who often gives a history of some recent infection of the upper respiratory tract is admitted to the hospital complain-

ing of cough, fever, and occasionally pain in the side. The onset, as a rule, is gradual, though it may be very sudden. Many cases are admitted with a diagnosis of influenza or bronchitis. The cough is usually dry in character and is often entirely absent, a feature which makes it difficult or impossible to collect a satisfactory specimen of sputum. The sputum itself is rather characteristic. It is usually of a white or yellowish color, quite viscid and mucopurulent. The rusty or hemorrhagic sputum of lobar pneumonia is rarely seen. The fever usually runs an irregular course, and considerable febrile periods succeeded by rapid oscillations, as in an active sepsis, appear at the onset. The pulse is comparatively slow in this early stage of the pneumonia, but is in proportion to the temperature. The respiratory rate is, however, proportionately high throughout. Pain in the side is a very inconstant symptom and when present is an additional cause of the inspiratory distress. Inspiratory pain is not usually long continued and few patients have required strapping or opiates because of it.

Physical Signs Before Onset of Empyema.—The physical signs before the onset of empyema are often indefinite. On percussion, areas of dulness may or may not be present at first. Moist crackling râles are nearly always to be heard, at times confused with the pleuritic friction rub, but typical bronchial voice and breathing are rather unusual signs at the onset of the pneumonia. More often the voice and breath sounds are faint. Furthermore, one must say that there are few distinctive signs or symptoms at the onset of the pneumonia which serve to differentiate cases which subsequently develop empyema from those that do not.

Physical Signs After Onset of Empyema.—In several instances patients have entered the hospital under the regimental diagnosis of empyema. Careful investigation of the history has, however, in all these instances shown a story of several days of indisposition and probable fever. Patients who have entered the hospital usually because of prostration and a slight febricula and before any physical signs indicative of either pneumonia or empyema appeared, have often developed under observation surprisingly early empyemas. Thus our group of streptococcus cases has shown a positive diagnosis of empyema possible in an average of 5.4 days after admission. When one takes into consideration the fact that three of these patients developed their pneumonia in the hospital as a secondary process two or three weeks after admission, the very early onset of streptococcus empyema is impressively demonstrated. Suffice it then to conclude that this empyema develops with surprising rapidity and often before a conclusive diagnosis of pneumonia, in addition to pleurisy, could be

made except by the assistance of the roentgen ray. It is therefore seen that these empyemas are imposed on, and do not merely succeed, the active stages of pneumonia. The prognostic significance of this fact must be apparent to all.

In our early experience with the disease we were surprised, in three instances, to find empyema at the postmortem where simple lobar pneumonia had been expected. In two of these cases the physical signs should certainly have given the diagnosis, and mere indolence on the part of the ward surgeon accounted for this failure. Careful analysis of the charts in these three cases, however, presented nothing of a symptomatic character which would lead any one unsophisticated in this epidemic to suspect the development of an empyema, for the picture was typically and solely that of a pneumonia. Nor was this finding limited to our early cases alone, for not seldom, even after we were keenly alive to the frequency of empyema, the needle and the roentgen ray have detected rapidly developing empyemas which were entirely unmarked by alterations in the clinical picture, and with strikingly few modifications in the physical signs.

One of the most constant and suggestive signs has been the appearance of profuse sweats, comparable in degree and in exhaustion to those of acute rheumatic fever. The entire surface of the body, more notably the head and the neck, are frequently beaded with large drops of sweat. These signs are unaccompanied by a chill, which is found to be a rather unusual symptom at any stage of these cases, and one which never appears but at the period of onset. Under onset we have mentioned the marked exhaustion which typifies these cases. This, however, is in no way characteristic of the empyema, since it may be also strikingly manifest in the simple streptococcus pneumonia. It is usually more pronounced when a purulent exudate is forming, or has formed, than when the pneumonia is uncomplicated. Where the exhaustion is very striking we have learned to be very constantly on guard and to apply the needle with even more diligence than ordinary, though not infrequently with negative results. Acceleration of the respiration is another suggestive sign, though of course in recognized pneumonia it can be considered as of only relative value; but there can be no doubt that as the pus begins to form there is a very perceptible increase in the respiratory rate, above that which may be attributed to the pneumonia alone, and with increase in rate is also to be found increased dyspnea and respiratory distress. There is nothing characteristic in the temperature and pulse curve in the early stage that suggests the onset of empyema. Of course, where it develops later in the pneumonia, when pulse rate and temperature are falling, an ascent in both appears. It rarely assumes a septic form, however.

In ordinary pleurisy and particularly in a process which so largely, as in these cases, involves the bases and diaphragmatic pleura, one is accustomed to consider abdominal rigidity a sign of considerable value, especially when, as is usually the case in this epidemic, it is monolateral at the onset. This sign has been strikingly absent in the cases which we present in this study. In but four of the cases do we recall this indication as demonstrable. It was often entirely absent even in instances in which we were able to demonstrate readily the fact that the diaphragmatic pleura was involved. Head zones of hyperesthesia is another frequent sign that one finds in cases of pleurisy of whatever origin, but which has not been present in our cases. Another negative sign which has impressed us very much has been the very general absence of or diminution in degree of the stabbing pain which is so generally complained of in the onset of pleurisy. This has not been frequent in our cases, even where the onset of pleural effusion seemed to take place synchronously with or but slightly later than the first pneumonic symptoms or signs. On the contrary, we have all been impressed with the frequency with which skin tenderness (not hyperesthesia) has been evident on even ordinarily vigorous percussion over the involved area. Not seldom this tenderness, which is a deep and not a superficial one, has largely determined us in selecting a point for needling.

Our study of the physical signs in general as regards this group of unusual cases has been disappointing and often the findings most difficult of explanation. As a result of great disparity between positive physical signs and lesions, our ward surgeon has been instructed to needle or fluoroscope even when all signs point away from the existence of pleural effusion. We both feel that we have "unlearned" far more physical signs of pleural fluid than we have perfected. All observers have been struck with the great frequency of skodaic resonance, and many times it has been most typical over areas from which the needle gave abundant fluid. Postmortem and roentgen-ray study of this sign has taught us to consider it as due in many instances to early pulmonary compression of more than the usual degree, because of the fact that the pleura in these cases was but little thickened, and the adjacent pulmonary tissue but little involved by consolidation. That this sign may be transmitted through a considerable amount of superjacent fluid has been demonstrated to us numerous times, and over areas where no transmission of abdominal tympany could be assumed. Probably for the same reason, breath sounds and vocal and tactile fremitus have been transmitted through massive exudates with great and deceptive distinctness. We have been forced to exaggerate alterations in these signs, or to totally ignore their appar-

ent significance. Doubtless the more limpid condition and less cell concentration of the fluid as compared with that of the antebellum conception of empyema has also something to do with the much modified physical signs. Beyond question the single physical sign which we have come to consider as of most value in the detection of these effusions is alteration in percussion. A high pitched note or the flattening of the customary resonance is a sufficient indication for a tap in these cases, and if the tap be a dry one a repetition is justified.

In six instances distinct and unmistakable pneumothorax has developed before the cases have been tapped, and in quite frequent instances minor degrees of this phenomenon appeared. In none of them could the usual explanatory causes be found present. There had been no possible injury to the thorax; no bacteria capable of causing gas formation were found in the fluid, and no possible cause of pulmonary laceration could be made out clinically, or in the three instances that came to necropsy. The amphoric splash and metallic tinkle of mingled fluid and air has come and gone in several typical cases also without a reasonable explanation. One hypothesis for these curious and surprisingly early manifestations is that they may be due to rupture of minute pulmonary abscesses, which thus allow the escape of air into the pleural cavity. Microscopic study lends some support to this theory.

In a discussion of the pathologic anatomy of the disease mention will be made of the frequent development of pleuropericarditis, and the very early appearance of this lesion is quite as remarkable as the appearance of the empyema itself. Usually when this process is present it becomes very early apparent from a primary pleuropericardial friction rub which is commonly so distinct as to become unmistakable. It diminishes, of course, as the effusion develops. As a natural sequence of this complication a pure pericarditis appears also with considerable frequency. Postmortem evidence shows that this first involves the parietal layer of the chamber, the visceral layer of the membrane only becoming involved later. Under our intensive method of study of the cases, the complication has only rarely escaped detection clinically. The amount of fluid which may thus accumulate in the sac may be very large — as much as 900 c.c., for example. The character of this fluid is precisely like that seen in the pleural cavities. First, it has a typical clear to turbid urine appearance, later on it becomes highly fibrinous, with the characteristic deposit of fibrin on both layers of the membrane and the ultimate transformation into pus of a clinical type. The bacteriology of the pericardial exudate coincides with that of the pleural fluid.

There are no signs or symptoms that appear in the pericardial complication which differ from those customarily seen in this condition. In two instances the pericardial sac was drained, once early in the course of the complication, once late after the fluid had become a thick and gelatinous pus. Both patients recovered.

Study of the total and differential white cell count has been very disappointing as a diagnostic measure. With the acknowledged existence of the pneumonia there is nothing shown suggestive of a developing exudate, nor of the fact that this fluid is of a highly septic character.

The blood pressure is that usually seen in pneumonias. Of course in fatal cases the pulse pressure becomes very much diminished as death approaches, and with it the usual tachycardia and cardiac arrhythmias which are common to the immediate premortem status.

The urine provides no data of an unusual character and nothing of a diagnostic value.

The roentgen ray has been used in almost all cases, in diagnosis; not so frequently for the demonstration of fluid as to indicate the extent and nature of the pulmonary process. In most cases so far as the demonstration of empyema is concerned the roentgen ray, particularly stereoscopic plates, have been most useful. It is much more necessary for the location of pulmonary disease. In several instances it has been misleading, indicating no fluid where the needle showed it to be present and less frequently the opposite fault has been found. The fluoroscope has not always been employed as a diagnostic routine for the reason that most of our patients have been so gravely ill that they could not be set up. It was soon found that satisfactory plates could only be obtained when the patient was raised up on a rack and kept in this position for a short period until gravity had caused the fluid to occupy a dependant part of the thorax. For a most satisfactory method of accomplishing this we are much indebted to our colleagues at Camp Devens, who first demonstrated their excellent practice to us. Our experience has shown us, however, that one may not depend absolutely on the roentgen ray in the diagnosis of empyema. In other instances it has misled us where the fluid was encapsulated at the left internal and posterior angle of the thorax, and its shadow obscured by that of the heart. The use of the roentgen ray is indispensable in the diagnosis of empyema, but it will not alone keep the lazy clinician out of trouble with the pathologist.

Frequent needlings have been most certain and more satisfactory in our hands. Where the puncture was to be made for diagnosis only, a fine hypodermic needle from 3 to 4 cm. in length attached to an ordinary 5 c.c. Luer syringe is used. The fluid in most questionable

instances is so limpid that it can be very readily obtained in this manner in sufficient quantity for bacterial and histologic diagnosis, and the pain caused by this needling is so slight that the patients do not object to frequent taps. We ordinarily do our aspirations with the Potain aspirator, but sometimes when the amount to be aspirated is small, an ordinary 20 c.c. glass syringe is used. We cannot commend the use of the needle too highly. It is indispensable in diagnosis.

Character of the empyema fluid: The pleural exudate when removed is usually light yellow, often with a greenish tinge, and in the early stages only slightly cloudy. Later in the disease it may take on a distinctly purulent character. Smears from the fluid show pus cells in large numbers, and large round or slightly flattened cocci arranged in short chains of from two to ten organisms. We have observed that the bacteria are much more numerous in the streptococcic empyema than in the pneumococcic empyemas. Cultures from the exudate on blood agar plates show, after twenty-four hours' incubation, many small, elevated, opaque, colonies of a pearl-gray color, each surrounded by a sharply defined zone of hemolysis. Subcultures in blood broth produce diffuse clouding of the medium, with a heavy sediment in the bottom of the tube. Rapid destruction of the blood cells takes place and the blood broth takes on a brilliant, claret-red color. Smears from the blood broth show chains of cocci similar in all respects to those seen in the smears from the pleural exudate.

The mortality rate in this group was very high, our experience in this respect corresponding to that met by clinicians in other camps. Of the thirty-six cases, twenty-two patients died, a mortality rate of 61 per cent.

(*b*). *Streptococcus Viridans Empyemas.*—In this group of cases cultures from both the sputum and the pleural exudate showed a streptococcus of the nonhemolyzing variety. There were found four cases of this type (Nos. 52-55). Clinically, these cases have differed in no respect from the *Streptococcus hemolyticus* cases. All four of these were cases of bronchial pneumonia, and the symptoms and signs of empyema were similar in every way to those of *Streptococcus hemolyticus* empyema. Three out of the four patients died.

(*c*). *Streptococcus Empyemas Following Pneumococcus Pneumonias.*—This very interesting group of mixed infections consists of nine cases (Nos. 56-65) and corroborates the findings of Cole and McCallum at Fort Sam Houston. In these cases the pneumococcus was cultivated from the sputum, but cultures from the pleural exudate gave streptococcus, either hemolyticus or viridans. Pneumococci of Type II, III and IV are represented in this group of mixed infections. There is also a case (Case 61) which we include in this group which

gave pneumococcus, Type IV, in the sputum, but *Staphylococcus aureus* in the exudate. It is possible, however, that in this case the staphylococcus infection developed after operation and drainage had been performed. The majority of these cases were frank lobar pneumonias. There were two cases diagnosed bronchopneumonia, and it may have been that in these two cases mouth pneumococci confused the bacteriologic picture. This was also a highly fatal group, six out of ten patients dying. Clinically, the empyema in this group possessed all the characteristics of the pure streptococcus type.

Summarizing these three subgroups, there were forty-nine streptococcus empyemas with thirty deaths, a mortality rate of 61 per cent.

3. *Sterile Empyemas.*—In addition to the sixty-five empyemas already mentioned, we have included in our study fifteen cases (Nos. 66-80) in which fluid of a purulent or semipurulent nature was removed from the pleural cavity, but from which cultures were sterile. In several of these cases gram-positive cocci were seen in smears from the fluid. They usually showed, however, some sign of disintegration and could not be cultivated even on blood medium. Ten of these empyemas were associated with pneumococcus pneumonias of the lobar type, and five patients died. Five cases were associated with streptococcus pneumonia and two of these patients died.

Blood Cultures.—Blood cultures were made on twenty of our empyema cases, with only three positive results (Nos. 7, 10 and 39). Two of these were pneumococcus cases and one *Streptococcus haemolyticus*. In the early part of the year, blood cultures were taken on every case of pneumonia, but when it was found that the results were almost universally negative this procedure was discontinued as a part of the routine examination. The clinical picture might lead one to suspect that this disease was one phase of a general septicemia. The character of the temperature curve, the pulse rate, the profound prostration, the rapid course of the disease and the high mortality all support this impression. The rare occurrence, however, of metastatic foci points strongly against this theory. Strangely enough, two out of the three patients in whom the blood culture was positive made uneventful recoveries.

PATHOGENESIS OF EMPYEMA

All of our cases of empyema have been associated with pneumonia, but in many of the streptococcus cases the pneumonic process has been relatively slight, as verified by physical signs, the roentgen ray and necropsies. Cases of *Streptococcus haemolyticus* empyema have been reported from other camps in which no evidence of con-

comitant pneumonia could be obtained, and such a phenomena seems possible in consideration of our own experience. It is quite certain that in many cases the empyema has far outweighed the pneumonia in clinical importance. It is probable, however, that in the majority of cases streptococcus empyema develops from a bronchopneumonia, the infectious organism being conveyed to the pleura either by the way of the lymphatics or by the direct extension of one of the small abscesses so frequently seen, through the pleural coat. The severity of the pneumonia may be a factor in the development of the empyema, but this is a difficult point to settle, since the onset of the empyema early in the course of the disease masks the real character of the pulmonary condition. It may be stated, however, that streptococcus empyema has usually appeared in those cases of pneumonia that have seemed to be severe infections.

The question if ward infections occur in this disease, that is, patients suffering from pneumonia of whatever type are likely to contract a streptococcus empyema from their associates in the ward or from streptococcus carriers, receives some confirmatory evidence from the fact that our group of cases includes nine instances in which a pneumococcus infection of the lung was followed by a streptococcus empyema. On the other hand, we have seen nothing clinically that would seem to substantiate this hypothesis, and since we have adopted careful methods of isolation of cases in the wards by means of screens and punctilious gowning, capping and veiling of attendants, nurses, physicians and convalescent patients, no change in the incidence of empyema has been evident. It is interesting to note that our camp was entirely free from streptococcus empyema until we received a large contingent of colored troops from another encampment said to have suffered much from this condition. This complication is no longer limited to "ultrabrunettes" with us at Camp Upton.

The likelihood of an autogenous infection from streptococci already in the mucous tract of patients before they contract the pneumonia seems to us a much more probable factor. This has received suggestive corroboration at Camp Upton from a series of cultures made during an epidemic of streptococcus pharyngitis in the convalescence of which a considerable number of streptococcus pneumonias developed.

PATHOLOGY

Altogether, twenty-seven of the empyema cases came to necropsy. Three of these (Cases 6, 9 and 10) were pneumococcus empyemas, one gave sterile cultures and the remaining twenty-three all showed streptococci in smears and cultures.

The three pneumococcus cases were associated with typical lobar pneumonia, with consolidation in the side involved. The fluid in all three of these cases was frankly purulent, and in one case there were pockets of pus between the lobes of the lung. One case was associated with acute vegetative endocarditis of pneumococcus origin. In all three cases the pleura was covered with a thick layer of fibrin, which could be readily removed from the underlying membrane.

The one post mortem case (Case 70) of empyema from which cultures during life had been sterile showed at necropsy pulmonary tuberculosis and tuberculous pleuritis.

The remaining group of twenty-three cases all showed streptococci in pleural exudate. Three of these cases (Cases 56, 62 and 64) belonged to the mixed group of infections. They had been classified from sputum examination as pneumococcus infection of the lungs. The cultures from the pleural exudate gave in two cases a nonhemolyzing type of streptococcus, and one case the hemolytic streptococcus. At necropsy all showed typical lobar pneumonia, but in addition, patches of bronchopneumonia were present in those portions not involved in the lobar process. In three other cases (Cases 53, 54 and 55) bacteriologic examination of both sputum and pleural exudate gave the nonhemolyzing or green streptococcus. All three of these cases showed a patchy type of consolidation and were classed as bronchopneumonias. The empyema in this group was of the sacculated type and the fluid was cloudy, yellow and full of flecks of fibrin. In two cases (Cases 54 and 55) which showed purulent pericarditis, the process was apparently an extension by direct contiguity from pleura to pericardium, for the pleura adjacent to the pericardium was extensively involved.

The third subgroup in this division is that in which the process in the lungs and the pleura was all of *Streptococcus haemolyticus* origin. There were seventeen of these cases that came to necropsy. Eleven were diagnosed as bronchopneumonia and six as lobar pneumonia. The empyema in this group was described as sacculated in half the cases; in the other cases the fluid was lying free in the pleural cavity. The fluid was sometimes cloudy and amber-colored and sometimes distinctly purulent. In the former group there were often a number of large, entirely separate pockets which did not communicate with one another. One such pocket was frequently found between the pericardial sac and the anterior flap of the left lung which lies over it. This probably accounted for the frequency of pericarditis in this group.

The lung on the affected side in these cases is covered with a fibrinous coat which varies in thickness with the age of the empyema. It is closely adherent to the pleura. The lungs in these streptococcus cases

have nearly all shown the changes described by Cole and McCallum as interstitial bronchial pneumonia. The lung is atelectatic, due to the compression caused by the fluid. On section the bronchioles stand out with remarkable distinctness and are usually filled with pus. The walls of the bronchioles appear thicker than normal and there is an over-growth of fibrous tissue throughout the organ which accentuates the fibrous trabeculae. The thickening about the bronchioles may be so marked as to give them the appearance of small tubercles or miliary abscesses. Even in those cases in which a part or all of a lobe is consolidated, these changes have been observed in other parts of the lungs.

Microscopic sections of the lungs in these cases show areas of bronchopneumonia around the bronchioles and an extensive infiltration of small round cells about the bronchioles and blood vessels. There is a marked tendency toward organization of the exudate in the alveoli, which consists of unusually dense fibrin, lymphocytes and desquamated epithelium.

The pleural covering has been converted into a thick coat of granulation tissue, on the surface of which there is a layer of fibrin and leukocytes. Small miliary abscesses have been observed in cases, sometimes occupying the site of a bronchiole and at other times situated so as to displace a number of the alveoli. In one case these minute abscesses were located about the small blood vessels.

OTHER PATHOLOGIC CONDITIONS ASSOCIATED WITH EMPYEMA

The only other pathologic condition which occurred with any frequency was suppurative pericarditis. This was found altogether in nine cases, eight of which were in the streptococcus series and one in the cases of mixed infections. In one other case a fibrinous pericarditis was found, and in this latter case it was easy to understand why the pericarditis accompanies the empyema so frequently. That portion of the parietal pericardium which lay in immediate contact with the left pleura was intensely reddened and covered with a fresh deposit of fibrin. The infection had apparently extended into the pericardium by direct contiguity, probably by way of the lymphatics. In quite a number of these infections of the pericardium a pocket of pus was found between the pericardial sac and the adjacent portion of the left lung.

Abscess of the lung was the next most common pathologic finding and was noted in five cases. These abscesses were usually small and multiple, but in one case there was a single large abscess located in the center of the consolidated area.

Infarcts were found in two cases (10 and 38), once in a pneumococcus empyema and once in a *Streptococcus hemolyticus* case.

Acute vegetative endocarditis was noted in one of the pneumococcus cases (Case 10), while acute general peritonitis (Case 46) and acute suppurative meningitis (Case 53) were each observed once, and each in connection with a streptococcus infection.

Bilateral empyema was noted in only two cases, once in a pneumococcus case and once in a streptococcus case.

It will be seen from this summary that in spite of the virulence of this infection it was usually confined to the lungs and pleura, with occasional involvement of the pericardium. This would seem to indicate, as already noted, that the disease is not essentially a septicemia.

TREATMENT

It has not been our original intention to attempt to consider this phase of the subject extensively in this paper. Perhaps our mortality rate in the streptococcus pneumonias should suffice as an excuse for this reticence on our part, but we do feel it necessary at least to outline what in our experience should not be done in the hope that it may be of assistance to others who are dealing with these same problems. At the outset we feel ourselves forced to say that the unfortunate interference of lay military commanders in the matter of necropsies must be held responsible to some extent for failures in treatment and the much longer and costlier method of forcing us to solve this problem by experiment rather than from the more exact knowledge which the postmortem alone gives to serious inquiring clinicians.

It is of course obvious that since most cases of streptococcus empyema develop very early in the course of pneumonia, it cannot do in case operative measures are decided on to use general anesthetics, nor does it seem wise to trust the after-treatment of such cases to surgeons alone. Entire cooperation must exist between the medical and surgical departments, and these patients, even though operated on, should be still considered as properly under medical charge.

In ordinary empyema of pneumococcus type we think there can be but little question that in the larger number of cases diagnosis should be followed by early operation. This older idea has been confirmed in our minds by such cases of this class as have occurred in this epidemic. As in the usual run of cases, operation has in most instances been followed by prompt benefit and reasonably early recovery. The results have been decidedly different in our cases of streptococcus empyema, as also in those so-called sterile empyemas which we believe are likewise of streptococcic origin.

In eleven of our twenty-two fatal cases in the *Streptococcus haemolyticus* group the men have been operated on, most of them in the relatively early stages of the empyema, and of the fifteen men who have recovered or are still in the hospital, but eight had a resection done. Study of this recovery list, however, has apparently shown that those patients operated on early have, almost without exception, died, while those in whom the operation has been postponed until the pus became thick and gelatinous (frequent aspirations in the meantime having been made), recovered.

As a result of our study of this group we have naturally arrived at the practice of withholding our cases from the surgeon until later in the course of the disease, when the pus has become thick with fibrin and cells.

We have felt that our better success since this method had been adopted has depended in part on the fact that when the pleural cavities are drained through the active stage of the pneumonia the rapid collapse of the diseased lung on the operated side has thrown an added strain on the unprepared heart, which has been a dominant factor in the cause of post operative death. Furthermore, when the waiting policy is pursued, not only may the pneumonia improve and the heart adjust itself to the strain thrown on it, but it has been our observation that the pleura becomes so thickened as a result of the exudate that the subsequent collapse of the lung following thoracotomy is less marked.

We may summarize our present procedure briefly as follows, but while our results are now better than formerly, we at the same time acknowledge that they are very far from satisfactory.

The case is carried as an ordinary case of pneumonia. As soon as the fluid is discovered (and with the persistent use of the needle and roentgen ray this is usually very early determined) the aspirated diagnostic specimen is examined by smear and culture. If the exudate is clear, notwithstanding the presence of streptococci, it is allowed to remain in the chest until it is apparent that the fluid is embarrassing respiration, in which case it is aspirated by the Potain aspirator. This aspiration is repeated as frequently as seems indicated, and careful watch is maintained on alterations in the character of the fluid. When it becomes thick and viscid, the case is deemed to have reached the stage for surgical intervention.

Meantime, of course, the general symptomatic treatment of pneumonia has been followed. As a rule, digitalis is given freely in the early stages and camphor, epinephrin, caffein, etc., are given as symptomatically indicated. The usual attention is given to elimination, to abundant aeration, and in suitable cases the patients are placed out of doors exposed to the sun and air. Temperature is controlled in part,

at least, by hydrotherapy and aerotherapy, and where much pain is suffered or when the patient coughs incessantly or becomes excitable, codein or morphin is used as indicated.

We are most anxious to attempt treatment of these cases by the use of an antistreptococcus serum, and steps in this direction are now being taken. We feel that until some protective mechanism is discovered we shall continue to find these cases most unfortunate problems in military medicine.

A marked improvement in results has followed the surgical treatment of these cases of hemolytic streptococcus empyema since they have been placed exclusively under the care of a single surgeon (Captain Perry), who has made a special study of this condition, and particularly of its surgical management.

SUMMARY

A highly virulent type of empyema has been prevalent at Camp Upton during the winter and spring months of 1918.

Eighty cases have been observed in a series of 300 pneumonias.

Fifteen of these were caused by the pneumococcus; fifteen others were sterile; the remainder of the cases were caused by a streptococcus, usually of the hemolytic type.

In this series of cases empyema has been constantly associated with pneumonia of either the bronchial or lobar type. Usually a bronchopneumonia has accompanied a streptococcus empyema, and a lobar pneumonia the pneumococcus empyemas.

In the great majority of cases the organism which has been found to be the causative agent in the pneumonia has also been isolated in pure culture from the pleural exudate. In nine cases, however, a pneumococcus pneumonia was associated with a streptococcus empyema.

The onset of the pneumonia and the empyema is apparently simultaneous in some cases.

This epidemic of empyema has been, in large part, independent of measles and other similar infections.

The clinical symptoms and the physical signs differ from those of classic empyema.

Diagnosis is frequently difficult by reason of the equivocal physical signs and the indefinite symptomatic picture. Diagnostic aspirations are the most certain means of discovery of the condition in its early stage. The roentgen ray stands second in diagnostic importance. Of the physical signs, alterations in percussion seem to be the most helpful.

The interstitial type of bronchopneumonia, recently described by Cole and MacCallum, is usually found associated with streptococcus empyema.

Fibrinopurulent pericarditis is the most frequent complication. Pyopneumothorax has also been observed in a number of cases.

The mortality rate is high and the prognosis is serious.

Medical treatment is essentially expectant.

The most efficacious method of surgical treatment and the correct time for its application are yet to be determined.

VOLUNTARY ACCELERATION OF THE HEART BEAT*

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Favill and White[1] have recently studied a person having the ability to increase the rate of the heart at will. This was the fourteenth of such persons to be reported (see Footnote 2). Electrocardiograms have been made of three of these persons, but only in the studies of Favill and White were the effects of atropin on the ability to accelerate observed. These authors, with others who have studied similar instances, were led to believe that the action of the accelerator nerves was the chief factor in the mechanism of this type of acceleration.

The following observations are reported in order to add another case to the series and because certain differences in results were obtained from those previously recorded.

The subject is a young medical student who is entirely healthy and is apparently free from all physical and neurotic defects. He has had no cardiovascular symptoms whatever and physical examination shows the heart to be of normal size and free from abnormal sounds and murmurs. Attacks of tachycardia have never been noticed. He discovered the ability to increase his heart rate voluntarily during the course in physiology in his freshman year and has practiced it only at times of making observations such as the following.

Electrocardiograms were made with an instrument of the Cambridge pattern so standardized that a deflection of 10 mm. was produced by a current of 1 m. volt. Continuous rolls of bromid paper were used so that the records covered fairly long periods of time. Radial pulse tracings were made with a Mackenzie polygraph, and blood pressure readings were made before and during periods of acceleration. The effects of large doses of atropin were tested.

During the period of acceleration there is a very slight increase in

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* From the Medical Clinic of the Peter Bent Brigham Hospital and the Harvard Medical School.

1. Favill, J., and White, P. D.: Heart, 1917, **6,** 175.

2. Koehler, M.: Arch. f. d. ges. Physiol., 1914, **158,** 579. Pease, E. A.: Boston Med. and Surg. Jour., 1889, **120,** 525. Tarchanoff, J. R.: Arch. f. d. ges. Physiol., 1885, **35,** 109. Tuke, D. H.: Illustrations of the Influence of the Mind on the Body in Health and Disease, Designed to Elucidate the Action of the Imagination, London, 1872. Van de Velde, Th. H.: Arch. f. d. ges Physiol., 1897, **66,** 232.

the rate and the depth of respiration (Fig. 3), and the pupils dilate moderately as recorded by other observers. No definite physical effort is made, but constant mental concentration must be maintained, which, after several closely repeated trials, becomes quite fatiguing.

Figure 1 shows a radial tracing and illustrates a typical period of acceleration of short duration. The rate begins to increase almost immediately following the word of command and reaches its maximum after about ten heart cycles. All our tracings show a decrease in amplitude of the pulse waves rather than an increase with marked dicrotism, as shown by Favill and White.[1]

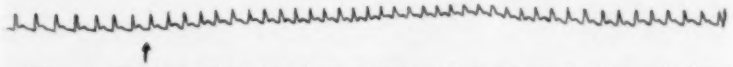

Fig. 1.—Radial tracing showing typical period of acceleration of short duration. Command to accelerate indicated by arrow.

There was a distinct rise in blood pressure with each acceleration with the exception of the effort at the height of the atropin effect, when there was a drop of 10 mm. from the reading made five minutes before. The latter reading, however, was 10 mm. higher than the first record made before the atropin was given. The greatest increase noted was one of 18 mm. accompanying an acceleration of 27 beats per minute. (See accompanying table.)

TABLE GIVING DATA OF AUTHOR'S CASE

Time, P. M.	Pulse Rate	Increase	Blood Pressure		Remarks
			Systolic	Diastolic	
4:20	69	..	120	70	
4:22	96	27	138	75	Voluntary acceleration
4:25	66	..	120	70	
4:27	..	..	...	..	Atropin 0.002 gm. subcutaneously
4:30	60				
4:55	66	..	120	70	Beginning dryness of mouth
5:10	74	..	115	70	Pupils slightly dilated; mouth very dry
5:15	86	12	130	75	Voluntary acceleration
5:20	94	..	130	70	Dizzy, slightly nauseated
5:25	102	8	120	70	Voluntary acceleration
5:35	..	..	...	..	Cardiogram taken. (Fig. 4.)
5:45	76	..	134	80	Dryness slightly less marked

Electrocardiograms of this student show no distinctive characteristics other than a slight notching of R and a diphasic T in the third lead. There is a definite, but not unusually marked, sinus arrhythmia (Fig. 2). During the periods of acceleration (Fig. 3) there was no change in the P-wave, in the P-R interval, nor in the distance from the beginning of R to the end of T. The amplitude of T was not changed. There was some rhythmic variation in the height of R both

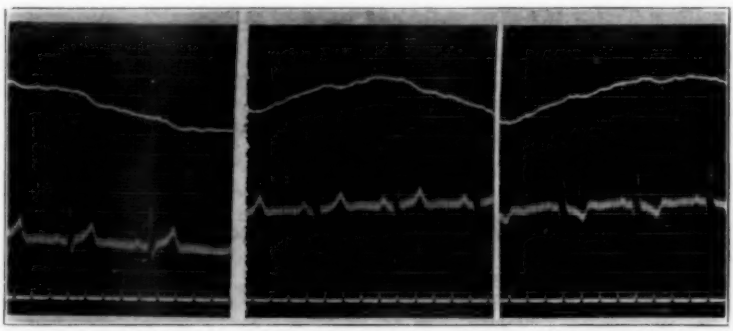

Fig. 2.—Leads I, II and III of subject at rest. Time in $\frac{1}{5}$ and $\frac{1}{25}$ second.

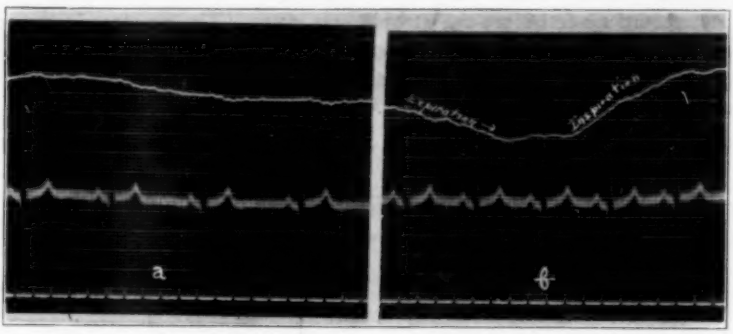

Fig. 3.—Lead II; *a*, just before command to accelerate; *b*, at height of acceleration. Line above electrocardiogram records respiratory movements obtained by pneumograph and tambour.

before and during the period of acceleration. The general average of the R deflections was slightly lower during the periods of acceleration, but by not more than one-tenth of the height preceding the increased rate.

After subcutaneous injection of 0.002 gm. of atropin sulphate the rate was increased from 69 to 94 beats per minute. Electrocardiograms taken at this time show a very slight increase in the amplitude

of T in the first lead and a correspondingly slight decrease in the height of R. No change in the distance from the beginning of R to the end of T could be made out. The sinus arrhythmia was almost, but not completely, obliterated. If one calculates minute rate on the shortest and longest cycles shown by the electrocardiogram at this time, a difference of 8 beats per minute results, which corresponds to the acceleration noted at the wrist as shown in the table. The ten beats preceding voluntary acceleration at the height of the atropin effect occurred at the rate of 80 per minute, the ten beats at the height of voluntary acceleration at 87 per minute, an increase of seven beats.

When respirations were forced without atropin the sinus arrhythmia becomes more marked as shown in Figure 5. If the rate were calculated on the basis of that seen at the beginning of inspiration,

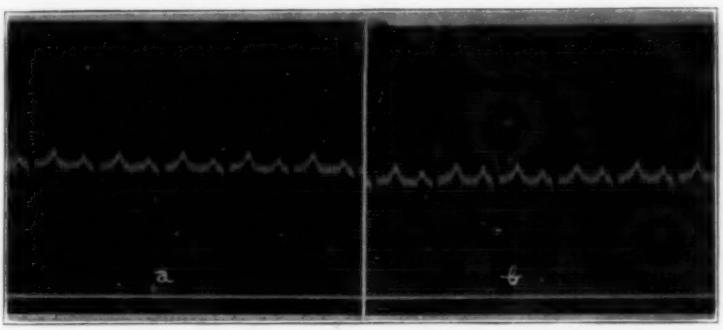

Fig. 4.—Lead II, sixty-eight minutes following injection of atropin. *a*, just before command to accelerate; *b*, at height of acceleration.

where it is most rapid, it would approximate 79 per minute. If calculated on the expiratory rate it would give approximately 54 beats per minute, or a difference of 25 beats. The greatest voluntary acceleration recorded in our observations was one of 27 beats per minute, which it would seem could be easily accounted for by vagus activity, assuming that sinus arrhythmia of the respiratory type is due to rhythmic changes in vagus inhibition. Pressure on the right vagus produced a prompt slowing of the heart rate from 72 to 48 beats per minute.

DISCUSSION

The identification of the mechanism involved in these cases is somewhat difficult and perhaps cannot be definitely attributed to either vagus or accelerator action alone, for there are probably no stages in the heart's activities in which both are not active to a greater or less extent. It would seem, however, that in this person our observations

point more to vagus than to accelerator domination during periods of acceleration. We have not been able to observe the marked decrease in the amplitude of R nor the increase in P and T during the increased rate as recorded by Favill and White and mentioned by Lewis and Cotton[3]—quoting Rothberger and Winterberg—as characteristic of effects of stimulation of the stellate ganglia. Nor have we obtained any decrease in the length of systole which was so marked in the experiments of Hunt[4] following direct stimulation of the accelerator nerves, and by Patterson[5] following intravenous injection of epinephrin.

Animal experiments have also shown that following stimulation of the accelerator nerves there is a prolonged latent period, from five to ten seconds, while the acceleration in these persons showing volun-

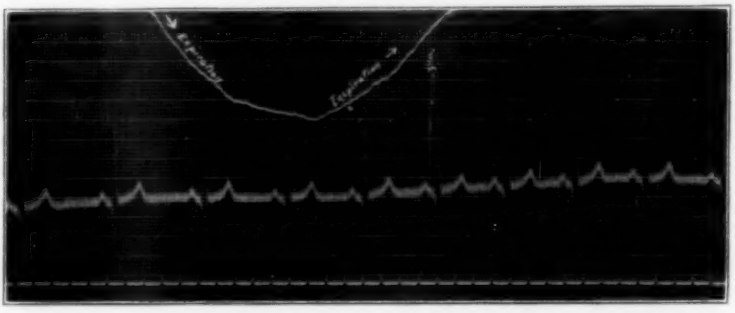

Fig. 5.—Electrocardiogram taken during period of forced respiration.

tary control begins almost immediately, reaching a maximum, it is true, after a few seconds of effort.

Then again, the degree of acceleration during our observations seemed to be definitely within the extremes of rate shown in a study of the normal sinus arrhythmia. The results following injection of atropin were quite at variance with those reported by Favill and White, who found no reduction in the ability to accelerate. As has already been pointed out, there was a definite and corresponding decrease in the sinus arrhythmia and the ability to acceierate at the height of the atropin effect in our observations. Had the atropin been given in sufficiently large dose completely to paralyze the vagus terminals we believe the ability voluntarily to change the rate would have been abolished or nearly so.

3. Lewis, Thos., and Cotton, T. F.: Proc. Physiol. Soc., June 28, 1913.
4. Hunt, R.: Am. Jour. Physiol., 1899, **11,** 395.
5. Patterson, S. W.: Proc. Royal Soc., 1915, **88,** 371.

Gasser and Meek,[6] after studying the mechanism of acceleration accompanying exercise, were led to conclude that the primary increase was due to a decrease in vagus inhibition, but that this was probably augmented "in times of great need" by accelerator influences. Our observations are entirely in accord with this view. It may be that those persons showing higher degrees of voluntary increase in rate may be able to add accelerator stimuli to a primary vagus release.

6. Gasser, H. S., and Meek, W. J.: Am. Jour. Physiol., 1914, **34**, 48.

ACUTE ENDOCARDITIS FOLLOWING WAR WOUNDS

INCLUDING NOTES OF HEART WEIGHT AND ARTERIOSCLEROSIS IN SOLDIERS *

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In a previous report[1] observations on the necropsies on eighty-seven soldiers who died in active service in France were recorded, reserving for separate study certain features of the pathology of the cardiovascular system. This seemed justifiable because of the relatively large number of cases of acute endocarditis observed. It is no new fact that acute endocarditis may accompany septicemia and pyemia, but surgeons and internists often regard the soldier as resistant to such complications and neglect this possibility in their treatment of the case. The experience of the writer in France has led to the belief that treatment can be successfully modified by a consideration of the changes in myocardium and renal parenchyma which may permanently handicap the soldier in after life. This study was taken up in the hope that light might be thrown on a subject by no means new, but as yet far from being satisfactorily explained.

As a corollary to the studies of acute endocarditis a study of the weight of the heart is presented and also a note on the occurrence of arteriosclerosis.

Acute endocarditis was observed in fourteen of the eighty-seven necropsies. There is no assurance that a similar percentage would be seen in a larger series of cases, but data should be collected. The number is large enough to be suggestive and to direct the attention of pathologists and clinicians toward minute observation of the valves in life and after death particularly in cases of septicemia or pyemia.

TYPE OF CASES

Of the fourteen cases showing acute valvular lesions, twelve were pure acute disease and two showed acute lesions superimposed on preceding chronic lesions. The twelve acute cases showed involvement of the aortic valve alone in five cases; the mitral, two cases; the pulmonary, one case; the tricuspid, one case; combined mitral and aortic, three cases. One case showed chronic mitral stenosis with

* Submitted for publication June 12, 1918.

1. Necropsy Service in a Military Hospital in the Field, appearing in Am. Jour. Med. Sc., June, 1918.

acute mitral and aortic lesions; one case showed chronic mitral and aortic stenosis with acute mitral lesions. The *Staphylococcus pyogenes aureus* was isolated in three cases, two of which were pyemias and one was a septicemia. The *Streptococcus pyogenes* was isolated in nine cases, two of which were pyemias and seven were septicemias. Two cases were clinically and pathologically septicemias, but were not demonstrated to be so bacteriologically. All had suffered serious primary wounds, five of which involved joints and four others of which involved other serous cavities. These wounds are irregularly distributed in regard to the valves attacked except that both the cases showing superimposition of acute on chronic lesions were penetrating wounds of the pelvis. In contrast to these figures, there were six cases of infected wounds of the joints which failed to show endocarditis, twenty-three cases of wounds of other serous cavities not including head wounds and forty-two cases of septicemia or pyemia without noticeable lesions of the endocardium.

AVERAGE DURATION OF ILLNESS

As to the duration of illness, one patient, a case of gas gangrene, succumbed in four days. The other thirteen patients were all ill one week or more; eight were ill more than two weeks; five more than three weeks; four, more than four weeks, and one was ill more than five weeks. The average duration of illness was eighteen days as compared with an average of seventeen days in forty-two septic cases without endocarditis.

TYPE OF ORGANISM FOUND

All the cases were obviously either septicemia or pyemias and the *Streptococcus pyogenes* was the predominant organism. One case showed perfringens in the blood after death, but all the work with this organism tends to show that it is not an invader of the blood stream during life. The case in question appeared to be septicemic as the result of pyogenic infection before the gas gangrene developed. It is not believed that *Bacillus perfringens* caused the acute endocarditis of this case.

AGE AND TERM OF SERVICE

The fourteen cases, as a group, averaged 29½ years of age and twenty-four and one-half months' service; somewhat greater in each instance than the averages for the entire group studied (27 years of age, twenty-two months' service). It may well be that the greater age and prolonged service might have reduced the resistance of these persons so as to expose them to this serious complication.

This information is summarized in Table 1.

TABLE 1.—Summary of the Study of Cases of Acute Endocarditis in Fourteen Soldiers

Lesion	Case No.	Age in Yrs.	Service in Mos.	Illness in Days	Wound	Disease	Organism
Acute aortic valvulitis	10	43	33	31	Buttock	Pyemia	Streptococcus
	12	22	19	50	Hip joint	Septicemia	Streptococcus
	25	34	25	16	Thigh	Septicemia	?
	30	28	36	22	Chest	Pyemia	Streptococcus
	51	35	15	17	Shoulder	Septicemia	Streptococcus
Acute mitral valvulitis	7	23	22	7	Knee joint	Septicemia	Streptococcus
	76	20	16	10	Chest	Septicemia	Streptococcus
Acute pulmonic valvulitis	2	22	24	29	Ankle joint	Septicemia	Streptococcus
Acute tricuspid valvulitis	9	29	12	28	Foot	Pyemia	Staphylococcus
Acute mitral and aortic valvulitis	14	29	36	7	Thigh	Septicemia	Streptococcus
	21	21	16	18	Knee and elbow joints	Septicemia	Streptococcus
	40	36	18	4	Leg	Gas gangrene	Perfringens
Acute superimposed on chronic valvulitis	20	34	25	14	Pelvis	Pyemia	Staphylococcus
	75	37	36	8	Pelvis	Pyemia	Staphylococcus

Note.—Streptococcus signifies a gram-positive organism in long chains. Staphylococcus signifies Staphylococcus pyogenes aureus. Pyemia indicates abscess formation in more than one organ.

TYPE OF LESION

The aortic lesions were in all cases extremely mild and might easily have been overlooked on less careful examination. It is of further interest that in all the aortic cases in which an organism was identified (six of the seven cases) the *Streptococcus pyogenes* was found, and this is true also of the acute mitral lesions. Both cases of acute valvulitis superimposed on chronic lesions were in association with *Staphylococcus pyogenes aureus*. The pure aortic cases show a rather high age incidence as compared with the other cases excepting the two patients who had acute and chronic lesions. This same group of men appeared to have been in active service somewhat longer than the other cases. From the mildness of the aortic disease and the apparently long duration of illness in these cases it might be assumed that this valve is somewhat more resistant to acute disease than are the other valves, but this view is more than counterbalanced by the large number of cases in which aortic disease appeared. It can be stated, however, that whereas acute aortic disease is common it does not become as severe and extensive as disease of the other valves, a fact in accordance with observations in civil life.

Of considerable interest is the occurrence in the fourteen cases of two cases with valvular disease of the right side of the heart only. This is extremely uncommon in adult life, but an examination of the data in these cases shows no explanation for their occurrence.

In only one case did the acute valvulitis appear to be of undoubted embolic origin, namely, the case of acute tricuspid disease, the lesion appearing as an ulcer in the middle of the valve flap and associated with what appeared to be an abscess in the substance of the valve. The case of pulmonic disease might have had a similar origin, for at the necropsy the lesions covered the ventricular surfaces of the leaflets and might have originated as emboli in the substance of the leaflets. All the other cases appeared to originate at the line of closure. According to the work of Bayne-Jones,[2] normal vascularization of the leaflets extends to the line of closure in the auriculo-ventricular leaflets, but only a short distance into the semilunar leaflets. Hence, lesions of the line of closure of the semilunar leaflets probably are not of embolic origin, whereas those of the line of closure of the mitral and tricuspid leaflets may or may not be.

CHRONIC VALVULAR LESIONS

There were four cases of chronic valvular disease without acute lesions, two of which were septicemias of rather short duration (five and ten days). The two cases of meningitis lived longer but were probably not septicemic. Of the two septicemic cases, one showed a sclerosis of the valve rather than a true chronic inflammatory process, leaving one case of chronic valvulitis with septicemia and without acute lesions as contrasted with two other cases with chronic valvulitis, pyemia and a superimposed acute lesion. This is in accord with the old view that a true chronic valvulitis predisposes to subsequent acute attacks (refer to Table 2 for summary).

TABLE 2.—Cases of Chronic Valvular Disease without Acute Lesions

Case No.	Age in Yrs.	Service in Mos	Illness in Days	Valve	Wound	Disease	Organism
36	24	19	5	Sclerotic aortic	Belly	Gas gangrene	Perfringens streptococcus
36	43	18	20	Chronic mitral	Chest	Streptococcus meningitis	No growth
64	24	18	28	Chronic mitral	Head	Staphylococcus meningitis	?
87	29	6	10	Chronic aortic	Thigh	Septicemia	Streptococcus

2. Bayne-Jones, S.: The Blood Vessels of the Heart Valves, Am. Jour. Anat., 1917, **21,** 449.

CARDIAC HYPERTROPHY

In several of the earlier necropsies it was thought that the heart was enlarged without noticeable cause. Scales were then purchased to try and determine if the life of the soldier induces a cardiac hypertrophy. It was not possible to weigh the cadavers so that the size was indicated as tall, medium or short; in some cases this was neglected.

The average weight of the heart in twenty-four men whose size was not noted was 305 gm. Excluding one heart of 420 gm. regarded as definitely hypertrophic, the average was reduced to 300 gm. Nineteen of these men had slight sclerosis of the aorta. The average service was twenty-three months and age 24 years. The average kidney weight 328 gm.

The average heart weight in twenty tall men was 344 gm. Excluding two hearts of over 400 gm., this was reduced to 336 gm. Fifteen of these men had slight sclerosis of the aorta The average service was twenty-five months and the average age 28 years. The average kidney weight was 374 gm.

The average heart weight in eighteen medium sized men was 322 gm. Excluding three hearts of more than 400 gm., this was reduced to 301 gm. Thirteen of these men had slight sclerosis of the aorta. The average service was twenty months and the age 28 years. The average kidney weight was 346 gm.

The average heart weight in ten small men was 265 gm., none exceeding 400 gm. Five of these men had slight sclerosis of the aorta. The average service was sixteen months and the age 24 years. The average kidney weight was 301 gm.

The foregoing information is summarized in Table 3.

TABLE 3.—SUMMARY OF THE STUDY AT NECROPSY OF THE HEARTS IN A SERIES OF SOLDIERS

Stature	Number of Cases	Heart, Weight in Gm.	Excluding Hypertrophy	Sclerosis	Service	Age	Kidneys, Weight in Gm.
No note	24	305	300	19	22	24	328
Tall	20	344	336	15	25	28	374
Medium	18	322	301	13	20	28	246
Small	10	265	265	5	16	24	301
Totals	72	314	305	52	22	27	342

INFLUENCE OF ARTERIOSCLEROSIS AND CHRONIC INTERSTITIAL NEPHRITIS

The importance of the influence of arteriosclerosis and chronic interestitial nephritis was considered and the cases grouped as follows: There were eighteen cases with both arteriosclerosis and chronic interstitial nephritis, whose hearts averaged 316 gm. in weight;

excluding three cases with hearts of more than 400 gm., the average was reduced to 283 gm. There were thirty-four cases with arteriosclerosis and without chronic interstitial nephritis, the average heart weight being 319 gm.; excluding two large hearts, this was reduced to 314 gm. There were only two cases with chronic interstitial nephritis and without arteriosclerosis, too few to present figures. There were fifteen cases without either arteriosclerosis or chronic interstitial nephritis, the average heart weight being 303 gm.; excluding large hearts, this was reduced to 295 gm (Table 4 shows this in summary).

TABLE 4.—SUMMARY OF THE INFLUENCE OF ARTERIOSCLEROSIS AND CHRONIC INTERSTITIAL NEPHRITIS ON HEART WEIGHTS

With Arteriosclerosis and Chronic Interstitial Nephritis		With Arteriosclerosis, without Chronic Interstitial Nephritis		Without Arteriosclerosis, or Chronic Interstitial Nephritis	
Number of Cases	Average Weight of Heart, Gm.	Number of Cases	Average Weight of Heart, Gm.	Number of Cases	Average Weight of Heart, Gm.
18	316	34	319	15	303
Excluding three large hearts.....	283	Excluding two large hearts.....	314	Excluding one large heart.....	295

As would be expected, the association of these two lesions is accompanied by greater heart weight than is the case when they are absent, but if the large hearts are excluded in making the average it would appear as if the arteriosclerosis were the more important change. Anatomically, the lesions were mild in both the cases of arteriosclerosis and chronic interstitial nephritis. Without functional studies of the cardiovascular system and renal sufficiency and with the variance in figures a conclusion is unjustified. No light was thrown on the variance of these figures by examining the age, service and stature of these cases, as the distribution was fairly even.

INFLUENCE OF AGE AND LENGTH OF SERVICE

The question of age and service was investigated taking the average of all the cases as the dividing line. There were thirty-six patients more than 27 years old with an average heart weight of 326 gm., excluding five large hearts, 300 gm., in contrast to thirty-four patients less than 27 years of age with an average heart weight of 305 gm., excluding one large heart, 301 gm. There were thirty-four patients with more than twenty-two months' service with an average heart weight of 350 gm., excluding three large hearts 324 gm., in contrast to thirteen patients less than 27 years of age and with less than twenty-two months' service, with an average heart weight of 279 gm., not including any large hearts. Table 5 gives a summary of these cases.

TABLE 5.—Summary of the Relation of Age and Length of Service in Their Effect on Heart Weights

Over 27 years old	326 gm.	Under 27 years	305 gm.
Excluding five large hearts	300 gm.	Excluding one large heart	301 gm.
Over twenty-two months' service	330 gm.	Under twenty-two months' service	293 gm.
Excluding four large hearts	316 gm.	Excluding two large hearts	284 gm.
Over service and age	350 gm.	Under service and age	279 gm.
Excluding three large hearts	324 gm.	No large heart	

It will be noted that, excluding the large hearts, there is no difference in weight in the two age periods, but that under the same condition the men who have served more than twenty-two months have hearts averaging 32 gm. heavier than their fellows of shorter service. In the case of thirteen men who were more than 27 years of age and

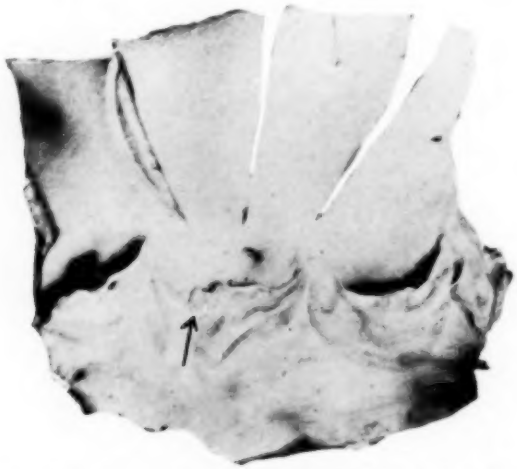

Fig. 1 (Case 21).—Aortic valve showing vegetations just above the line of closure. This case also had acute mitral disease.

had more than twenty-two months of service, the hearts averaged 71 gm. greater in weight than in the case of thirteen others who were less than 27 years of age and had less than twenty-two months' service; excluding large hearts the difference in the two groups was 45 gm. The stature of these men was considered, but appeared to be fairly evenly distributed. It, therefore, appears that long service and increased heart weight go hand in hand. If to the long service there is added greater age, the increase in weight becomes more marked.

Hearts weighing 400 gm. or more have been regarded as examples of hypertrophy and deducted from the total in reaching averages. Six hearts fell in this group and all but one could be accounted for by

other lesions in the body. Three of these were associated with a chronic interstitial nephritis, which although of mild degree might have been sufficiently diseased functionally to have produced heightened blood pressure. All of these showed in addition a slight sclerosis of the aorta. One case showed the abnormality below the aortic orifice described elsewhere, which might easily have led to hypertrophy and in addition a slight sclerosis of the aorta. One other case showed only arteriosclerosis as a possible cause for the hypertrophy. One patient (Case 69) had a heart of 420 gm. with no arteriosclerosis, no valve lesion, no chronic nephritis or any other apparent cause for enlargement. His body is described as that of a "tall, heavily muscled, well nourished man." He had a liver of 2,685 gm., showing only passive congestion, a soft flabby spleen of 285 gm., apparently normal kidneys weighing 410 gm. He was a Scottish guardsman who had

Fig. 2 (Case 10).—Aortic valve showing erosion and vegetations below the corpus Arantii.

served thirty-six months. Compared to the weight of the other organs the heart is not materially enlarged and doubt is left in one's mind as to whether or not this case should be classified as a hypertrophy.

When it is noted that the greatest weight recorded in the series is 475 gm. and that next to that are two hearts of 420 gm., one of these being a doubtful hypertrophy, it can be seen that definite hypertrophy of the heart played a very small part in the gross morbid anatomy of these soldiers.

These six cases averaged 37 years of age and twenty-seven months of service, distinctly above the average of 27 years of age and twenty-two months' service. This may be taken to support the suggestion that older men of long service tend to have larger hearts than the opposite group.

Table 6 gives a summary of these data.

TABLE 6.—Summary of the Findings at Necropsy in Six Cases Classed as Hypertrophy of Heart

Case No.	Age in Yrs.	Service in Mos.	Heart Wt., Gm.	Valve Lesion	Sclerosis Aorta	Kidney Wt., Gm.	Kidney Lesion	Disease	Stature
14	29	26	420	Acute aortic mitral valvulitis	+	430	Chronic interstitial nephritis	Streptococcus septicemia	No note
46	26	32	410	None	+	420	Cloudy swelling	Streptococcus meningitis	Tall
51	35	15	400	Abnormal acute aortic	+	356	Cloudy swelling	Streptococcus septicemia	Medium
54	48	27	475	None	+	380	Chronic interstitial nephritis	Gas gangrene	Medium
56	45	18	400	Sclerotic mitral	+	450	Chronic interstitial nephritis	Chest wounds	Medium
69	40	26	420	None	—	410	Normal	Chest wounds; perfringens	Tall

ARTERIOSCLEROSIS OF THE AORTA

This condition was noted in sixty-two of a total of eighty-one cases in which a note was made on the aorta. This was practically always slight, appearing usually as narrow white firm streaks longitudinally arranged throughout the length posteriorly, resembling a little the streaks of fatty change seen in the aortas of children dying from acute infection but being white and definitely fibrosed. A few of these showed slight fatty changes, but none showed definite calcification. It is not likely that this change can be accounted for by the acute infections from which the men died; it seems more reasonable to attribute the change to some other cause.

Coronary sclerosis was present in five cases, one of which showed also a sclerosis of the mitral valve. Sclerosis of the cerebral arteries was noted in one case of seventy-seven cases examined.

Averages were estimated of the age and term of service of sixty-two patients who showed sclerosis of the aorta and nineteen patients who failed to show it and the resulting figures were the same in each, namely, 27 years of age and twenty-two months' service. It is therefore unlikely that army service or the age of the soldier played any important part in the occurrence of the arteriosclerosis and that its cause must be sought elsewhere.

SUMMARY AND CONCLUSIONS

In summary, it may be stated that in spite of the fact that soldiers represent a group of men selected for superior physique, acute valvu-

litis is an important complication of septicemias and pyemias following war wounds. The men developing this complication are somewhat older and of longer service than the average of the entire group studied. The situation of the wound has little to do with this complication, except that wounds of joints form a larger percentage in the group of acute valvulitis cases than is true of the entire group. The *Streptococcus pyogenes* is an important organism, but is not more frequent in the smaller than in the entire group of cases. In one case embolism of the valve vessels seems to have been a cause, and in one

Fig. 3 (Case 51).—Aortic valve showing vegetations as indicated by the upper arrow and anomaly as indicated by the lower arrow.

other it is a possible cause. The aortic leaflets are the most commonly affected and at the same time show the least marked lesions.

The weight of the heart appears to be greater in men of long service and in older men, the difference being accentuated in men when greater age and longer service coincide. It is therefore tentatively concluded that long service in the army probably leads to an increase in the weight of the heart, and that this change is more marked in men above the average age of this series of soldiers.

It cannot be demonstrated that the life of the soldier leads to the development of arteriosclerosis.

List of Cases of Acute Valvulitis

I. ACUTE AORTIC VALVULITIS

Case 10 (Fig. 2).—The patient, aged 43, had been in the service thirty-three months. He was admitted to the casualty clearing station with shell wound of the buttock and fracture of the great trochanter. He was ill thirty-one days, a large abscess of buttocks developed and five days before death a dry pleurisy of the left side. The necropsy was performed fourteen hours after death and revealed extensive suppuration of thigh extending up to origin of psoas major but not involving hip joint. The heart was soft and flabby with normal valves except that one aortic leaflet showed in the middle of the ventricular surface a small erosion surrounded by very minute soft white vegetations. There was also acute fibrinous pleurisy, acute purulent bronchitis, septic infarct of lung, acute splenic hyperplasia, cloudy swelling of kidneys. Direct smear from psoas muscle showed only streptococci in unusually long chains. Direct smear from septic infarct showed a mixture of organisms, the streptococcus predominating.

Fig. 4 (Case 76).—Mitral valve showing vegetation as indicated by the arrow; chordae tendineae enmeshed in vegetation.

Case 12.—The patient, aged 22, had been in the service nineteen months. He was admitted to the casualty clearing station with shell wound of the buttock involving the sciatic nerve, with inability to extend the toes. During an illness of fifty days hemorrhage occurred, also edema of the thigh, and extensive suppuration of the thigh involving the left hip joint and following the psoas major to within 4 cm. of the diaphragm. At necropsy, fifteen and one-half hours after death, the heart was "small, soft and flabby with pallid friable muscle; the aortic leaflets revealed numerous extremely minute soft white vegetations along the line of closure; other valves normal." There was acute fibrinous pleurisy, bronchopneumonia, cloudy swelling of liver, hyperplasia of splenic follicles, acute pseudomembranous colitis and acute hemorrhagic nephritis. Cultures from the heart blood showed *Streptococcus pyogenes.*

CASE 25.—The patient, aged 34, had been in the service twenty-five months. He was admitted to the casualty clearing station with shell wound of the hip grooving the great trochanter. During an illness of sixteen days all the symptoms of a septicemia developed. At the necropsy, four hours after death, the heart "weighed 220 gm. and was normal except for the presence of a pinhead-sized vegetation on the right posterior leaflet of the aortic valve immediately below the corpus Arantii." There was also marked suppuration of thigh, passive congestion, edema and healed tuberculosis of lungs, cloudy swelling of the liver, submucous petechiae of stomach, follicular and general acute splenic hyperplasia and acute nephritis. Cultures from the heart blood were contaminated.

CASE 30.—The patient, aged 28, had been in the service thirty-six months. He was admitted to the casualty clearing station with a penetrating shell wound of chest. During an illness of twenty-two days pneumothorax developed, also hemothorax, phlebitis of right leg, purulent peritonitis, and from the chest a pure culture of *Streptococcus pyogenes* was obtained. At the necropsy, thirteen hours after death, the heart "weighed 345 gm., was soft and flabby and shows moderate dilatation of right side; the left posterior leaflet of the aortic valve revealed on the left half of its line of closure two pinhead-sized white fairly firm vegetations fairly well attached." There was also bilateral acute

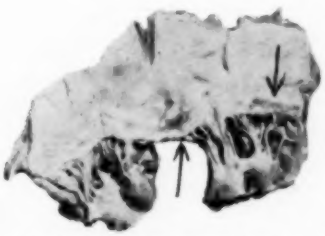

Fig. 5 (Case 20).—Mitral valve showing vegetations as indicated by the arrows.

fibrino-purulent pleurisy, hypostatic pneumonia, acute purulent peritonitis (metastatic) marked cloudy swelling of liver, acute hyperplasia of spleen with multiple infected infarcts and acute nephritis. Direct smears from the right pleura and belly showed numerous long chains of gram-positive streptococci which were outgrown in cultures by contaminations. This case is regarded as a streptococcus pyemia.

CASE 5 (FIG. 3).—The patient, aged 35, had been in the service fifteen months. Admitted to the field ambulance with extensive shell wound of left shoulder. During an illness of seventeen days gas gangrene developed, and the left upper extremity was amputated. At necropsy, seven hours after death, the heart "weighed 400 gm., showed considerable dilatation of right side, contained firm clot and frothy blood; aortic leaflets showed numerous extremely minute soft white vegetations along the line of closure; other valves normal; extending from the junction of the large mitral leaflet and left posterior aortic leaflet to a point on the septum just below the right posterior aortic leaflet was a band of fibrous tissue 2 mm. in thickness and about 15 mm. long, which widened in the middle to form a generally spherical sac about 7 mm. in diameter with an opening about 4 mm. in diameter; the septal end of this band was continued in a heavy band of muscle about 4 mm. in diameter not completely separated from the septum and extending vertically downward for 2.5 cm." The other organs showed the usual changes of gas gangrene. From the heart blood there were isolated *Streptococcus pyogenes* and *Bacillus perfringens.*

II. ACUTE MITRAL VALVULITIS

CASE 7.—The patient, aged 23, had been in the service twenty-two months. He was admitted to the casualty clearing station after "lying out" four days with shell wounds of left leg, left wrist and back, without any evidence of gas gangrene. He was ill seven days and died suddenly. The necropsy was performed eighteen hours after death and showed in addition to the wounds an acute suppurative inflammation of the left knee joint. There was no evidence of thrombosis or embolism in the femoral veins, coronary, pulmonary or cerebral arteries. The heart was described as "somewhat soft and flabby showing no dilatation of the left side but marked dilatation of entire right side; both sides filled with firm current jelly clot; on the posterior leaflet of the mitral valve at its line of closure were three minute, white, soft, acute vegetations." There was passive congestion of the lungs, cloudy swelling and passive congestion of the liver, acute splenic hyperplasia and acute hemorrhagic nephritis. From the knee joint there was isolated the *Streptococcus pyogenes.*

CASE 76 (FIG. 4).—The patient, aged 20, had been in the service sixteen months. He was admitted to the field ambulance with shell wound of back. At the casualty clearing station he had hematuria and vomiting; abdominal

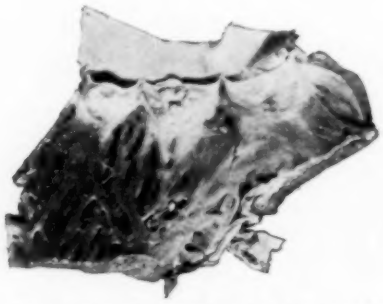

Fig. 6 (Case 2).—Pulmonic leaflets showing massive vegetation.

section revealed no visceral injury but retroperitoneal and intraperitoneal hemorrhage. At the base a retroperitoneal abscess was opened and drained followed by left empyema. He died after an illness of ten days. At necropsy, twenty hours after death, it was found that the wound had penetrated the lower part of chest and had split the lower pole of the left kidney. "Heart weighed 235 gm., showed a firm musculature and appeared to be normal except that the auricular surface of the right half of the posterior mitral leaflet was practically covered by a mass of small vegetations, soft, loosely adherent and salmon colored; the neighboring part of anterior leaflet showed a similar vegetation 2 mm. in diameter; other valves, coronaries and foramen ovale were normal." There was also a left sided empyema, acute purulent bronchitis, cloudy swelling of liver and kidneys, follicular hyperplasia of spleen and wound of kidney with practically no suppuration. Cultures from the heart blood revealed pure growth *Streptococcus pyogenes.*

III. ACUTE PULMONARY VALVULITIS

CASE 2 (FIG. 6).—The patient, aged 22, had been in the service twenty-four months. He was admitted to the casualty clearing station with shell wounds of left thigh, left ankle, left buttock and face. At the base hospital it was found that the ankle wound penetrated the ankle and tarsal joints and the

thigh wound was associated with a fracture of the femur. He was ill twenty-nine days, during the course of which an abscess of left arm developed, also two abscesses of the thigh, cellulitis of the left ankle and bed sores. The necropsy was performed twenty hours after death and the heart was described as follows: "of about normal size, soft and flabby, shows slight general dilatation; all valves normal except the pulmonary, all three leaflets of which show on the ventricular surface extensive flat, white, soft, easily detachable vegetations covering the entire leaflet and extending slightly onto the wall of the septum, and showing three minute vegetations on the intima of the pulmonary artery." There was associated miliary abscesses of the lungs, bronchopneumonia, cloudy swelling of liver, acute splenic hyperplasia and acute nephritis. From the lung abscesses there was isolated the *Streptococcus pyogenes* and a staphylococcus.

IV. ACUTE TRICUSPID VALVULITIS

CASE 9 (FIG. 7).—The patient, aged 29, had been in the service twelve months. He was admitted to the casualty clearing station with "inflammation of connective tissue" of left foot and doubtful pleurisy of left side. At the

Fig. 7 (Case 9).—Tricuspid valve showing triangular ulceration in the posterior cusp.

base hospital it was found that the "inflammation of connective tissue" had followed a blister of the left instep developing on a long march. He was ill twenty-eight days, developing cellulitis of entire left lower extremity with inguinal lymphadenitis, left subacromial bursitis and multiple subcutaneous abscesses. The necropsy was performed fourteen hours after death and revealed in addition to the above features, acute suppurative inflammation of the ankle joint particularly at the astragalo-scaphoid junction and gangrene of the great and second toes. The heart was "soft and flabby with pallid muscle, normal valves except that the posterior leaflet of the tricuspid valve showed, near its attachment to the ring, a horizontal linear abscess 10 by 2 mm. in the substance of the valve, over which the auricular surface showed a group of minute, soft, white vegetations covering an area 4 by 5 mm." The lungs revealed one hemorrhagic infarct and a large number of small septic infarcts and abscesses, some of which are partially encapsulated, local acute fibrinous pleurisy, cloudy swelling and passive congestion of liver, acute hyperplastic splenitis, acute suppurative nephritis, occluding thrombo-phlebitis of left femoral veins. The heart blood showed pure culture of *Staphylococcus pyogenes aureus* and this organism predominated in direct smears from abscesses in lungs, kidneys, thigh wound and thrombus of vein.

V. ACUTE AORTIC AND MITRAL VALVULITIS

CASE 14.—The patient, aged 29, had been in the service thirty-six months. He was admitted to the casualty clearing station with shell wound and compound fracture of the right thigh, and superficial wounds of the leg, abdomen, chin and head. During an illness of seven days signs of fracture of the skull and pneumonia developed. At necropsy, eleven hours after death, "the heart weighed 420 gm., showed a thick, firm left ventricle and moderately dilated right side; the mitral leaflets showed numerous small clusters of minute, white, soft, firmly attached vegetations extending along the line of closure; the aortic leaflets showed less numerous similar vegetations along the line of closure particularly marked on the left posterior leaflet." The skull showed fracture with extensive subdural hemorrhage, the lungs acute purulent bronchitis and extensive confluent bronchopneumonia, the liver cloudy swelling and fatty metamorphosis, the kidneys cloudy swelling superimposed on slight chronic interstitial nephritis. Cultures from the heart blood showed pure growth *Streptococcus pyogenes.*

Fig. 8 (Case 75).—Mitral stenosis showing superimposed acute vegetations.

CASE 21 (FIG. 1).—The patient, aged 21, had been in the service sixteen months. He was admitted to the casualty clearing station with shell wounds penetrating right elbow joint, right knee joint and buttock. During an illness of thirteen days the patient developed infection of knee and elbow joints and finally a meningitis. At necropsy, twelve hours after death, the "heart weighed 300 gm., was markedly dilated on the right side; the aortic leaflets showed very minute soft white vegetations along the line of closure; the posterior leaflet of the mitral showed four such vegetations at the middle of the line of closure; left ventricular muscle was firm, and heart was otherwise normal." There was also acute purulent cerebral meningitis, passive congestion of lungs, liver and kidneys and slight chronic interstitial nephritis. Cultures from the brain and the heart blood showed pure growth *Streptococcus pyogenes.*

CASE 40.—The patient, aged 36, had been in the service eighteen months. He was admitted to the field ambulance with shell wound of the right leg, left knee and right arm. During an illness of four days clinical signs of a streptococcus septicemia developed, and gas gangrene of right leg for which an amputation was made in midthigh. At the necropsy, fourteen hours after death, the heart "weighed 365 gm., was of doughy consistence with epicardial congestion and hemoglobin staining of the endocardium; anterior and right posterior leaflets of aortic valve showed several red, soft, very minute vegetations on the corpora Arantii extending slightly along the lines of closure; similar vegetations were found at the right junction of the mitral leaflets approximately in the position of the line of closure." There was also gas gangrene of the right thigh with the incident softening of all the organs and a chronic interstitial nephritis. Cultures from the heart blood showed no aerobic growth; anaerobically, *Bacillus perfringens* was found.

VI. ACUTE SUPERIMPOSED ON CHRONIC VALVULITIS

CASE 20 (FIG. 5).—The patient, aged 34, had been in the service thirty-five months. He was admitted to the casualty clearing station with shell wounds of the right buttock and left elbow. During an illness of fourteen days, there were two hemorrhages from the buttock wound and bloody stools (no perforation of the gut). At necropsy, two and a half hours after death, the "heart weighed 320 gm., and showed marked dilatation of the entire right side with slight hypertrophy of the left auricle; mitral valve showed fibrosis, adhesion, slight retraction of leaflets and adhesion with slight shortening of chordae tendineae; along the line of closure were numerous millimeter-sized, soft, light yellow vegetations; the stenosis was moderate, the orifice measuring 6.5 cm.; the aortic leaflets were normal except that along the line of closure of each leaflet there were a few vegetations similar to those on the mitral; valves of the right side were normal." There was, in addition, generalized icterus, acute splenic hyperplasia with multiple hemorrhagic infarcts, acute nephritis, acute fibrinopurulent pelvic peritonitis, acute pseudomembranous enterocolitis. Cultures from the heart blood showed pure growth *Staphylococcus pyogenes aureus.*

CASE 75 (FIG. 8).—The patient, aged 37, had been in the service thirty-six months. He was admitted to the casualty clearing station with superficial wound of chest and penetrating wound of pelvis not involving the gut. During an illness of eight days signs of pneumonia developed. At necropsy, four hours after death, the heart "weighed 350 gm., and showed slight hypertrophy of the left auricle; the mitral leaflets were thickened, somewhat retracted and adherent, associated with thickening and adhesion of the chordae tendineae; at the right junction of the leaflets on the auricular surface was a mass of dark brown, soft, firmly adherent acute vegetations 5 mm. in diameter; aortic leaflets were diffusely thickened, not retracted but showed adhesion of right posterior and anterior leaflets as far as the corpora Arantii, associated with stiffening and calcification; other valves, coronary arteries and foramen ovale were normal." There was also multiple septic infarction of the lungs, bronchopneumonia, acute fibrinous pleurisy, acute splenic hyperplasia and embolic abscesses of the kidneys. Cultures from the heart blood showed pure growth *Staphylococcus pyogenes aureus.*

PATHOLOGIC REPORT ON FORTY-THREE CASES OF ACUTE POLIOMYELITIS *

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The morbid anatomy of acute poliomyelitis has received careful and painstaking study by a number of European pathologists.

Rissler[1] was the first to describe the anatomic changes in the central nervous system, with a report of three cases, in 1888. The changes described were confirmed by a number of other students of the disease, chief among whom are Wickman[2] with a report of fourteen cases, Harbitz and Scheel[3] with nineteen cases, and Strauss[4] with eight cases.

These anatomic studies are confined chiefly to the nervous elements of the body, comparatively little attention having been paid to the other organs. Flexner, Peabody and Draper[5] studied eleven acute cases with special reference to the changes in the organs other than the central nervous system. They found constant changes in the lymphatic structures throughout the body and called attention to focal degenerative lesions in the liver. The changes in the lymphatic tissues consisted chiefly of hyperplasia of the reticular and endothelial cells.

Though the changes in the central nervous system of acute poliomyelitis as described by Rissler have been confirmed by all subsequent workers in this field, two schools of opinion have developed as to the interpretation of these changes. One group, headed by Rissler, believes that the nerve cell destruction is the primary change and that the cell reaction or inflammatory change has been called forth by the presence of the virus in the affected part. Mönckenberg[6] and Cassierer[7] agree with Rissler, inasmuch as they have studied cases in which there were marked nerve cell destruction with a minimum of interstitial reaction. Wickman,[2] Harbitz and Scheel[3] and others consider that the interstitial process is the primary stage and that the nerve cell

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* From the Bureau of Laboratories, Department of Health.

* This report was ready for publication in January, 1917, but was delayed on account of technical difficulties. In the series of articles on Poliomyelitis in THE ARCHIVES, September, 1917, a part of the first article was incorrectly headed Part II, Pathologic Studies.

1. Rissler, John: Nord. Med. Ark., 1888.
2. Wickman, Ivan: Nervous and Mental Disease Monograph, Series 16.
3. Harbitz and Scheel: Deutsch. med. Wchnschr., 1907, p. 48.
4. Strauss, J.: Arch. Pediat., August, 1910.
5. Flexner, Peabody and Draper: Jour. Am. Med. Assn., 1912, **58,** 109.
6. Mönckenberg, J.: München. med. Wchnschr., 1903.
7. Cassierer, R.: Neurol. Centralbl., 1898.

degeneration is secondary to the interstitial changes. Wickman has never found ganglion cell destruction without interstitial lesions. On the other hand, he has found interstitial changes without nerve cell degeneration. Harbits and Scheel state further that the disease is a blood borne infection, the virus lodging first in the meninges, and that it spreads from this site to the nervous tissue proper.

Forssner and Sjövall[8] first called attention to the importance of neurophagocytosis in the production of the histologic picture of this disease.

The epidemic of the summer of 1916 furnished the opportunity for the postmortem study of forty-three patients who had acute poliomyelitis, forty-one of whom died in the acute stage. Thirty-five were cases from the Willard Parker Hospital, and six were in private residences. Material[9] from two were sent to the laboratory for diagnosis. Eight cases other than poliomyelitis came to the necropsy table from the poliomyelitis wards. Four of these proved to be tuberculous meningitis; one lobar pneumonia; one congenital heart disease; one purulent pericarditis, purulent pleuritis, bronchopneumonia and general pyemia; one, intracranial hemorrhage.

The poliomyelitis cases as to sex, age and duration of illness are divided as follow:

Age	Number
Up to 1 year	8
1 to 2 years	8
2 to 3 years	13
3 to 5 years	2
5 to 10 years	4
10 to 16 years	1
Over 16 years	5

Up to and including 5 years, there was a total of 31, or 75.5 per cent.

Males, 28; females, 13.

Duration of Illness	Number
3 days	10
4 days	5
5 days	6
6 days	5
7 days	5
8 to 11 days	4
Over 12 days	4
Undetermined number of days	2

Thirty-one, or 75.5 per cent. of the patients died within the first week after onset.

The clinical classification as to types is based on the evidence of anatomic lesions. Thus, all cases exhibiting involvement of the lower motor neuron were called spinal cases. These were again divided

8. Forssner and Sjövall: Ztschr. f. klin. Med., 1907.
9. No history obtained of sent-in cases.

TABLE OF GROSS AND MICROSCOPIC CHANGES

No.	Name	Sex	Age in Years	Duration of Illness, Days	Type of Case	Gross Changes					Microscopic Changes					Remarks
						Brain	Cord	Mes. Node	Peyer's Patches	Spleen	Brain	Cord	Mes. Node	Peyer's Patches	Spleen	
1	R. S.	♀	1 6/12	11	Ascending spinal	++	++	+	?	++	++	++	+	+	+	
2	R. X.	♀	1 1/12	7	Upper spinal	+	+	−	−	−	+	++	−	−	−	
3	G. B.	♀	1 7/12	6	Upper spinal	+	+	+	±	+	+	+++	+	+	+	
4	M. F.	♂	2 6/12	3	Upper spinal	+	−	?	+	−	+	++	+	+	+	
5	C. P.	♂	8/12	6	Ascending spinal	++	?	−	+	+++	+	+	+	+	++	
6	J. N.	♂	2 6/12	3	Upper spinal	++	+	+	±	+	+	++				
7	I. S.	♂	3	4	Upper spinal	++	+++	+	+	++	±	+	−	−	−	
8	M. L.	♀	15 6/12	5	Ascending spinal	+++	?	−	−	−	+	+	..	..	..	Partial necropsy
9	E. C.	♂	7/12	6	Ascending spinal	±	+	+	+	−	+	+	+	−	−	
10	M. D.	♂	2 6/12	7	Upper spinal	+	+	++	+++	−	+	+	+	+	+	
11	I. F.	♂	2	5	Upper spinal	++	++	−	−	−	+	+	..	..	..	Partial necropsy
12	G. W.	♂	21	9	Ascending spinal	+	++	−	−	−	+	++	−	−	−	
13	N. H.	♀	1 11/12	10	Ascending spinal	++	++	+	+	−	+	++	−	−	+	
14	A. L.	♂	2	7	Ascending spinal	++	..	−	?	+++	+	++	−	−	+	
15	A. R	♂	8	4	Cortical	++	..	++	++	−	..	.	..	..	..	Sections lost
16	A. L.	♀	2 6/12	?	Upper spinal	+	..	−	++	−	+	++	±	±	±	
17	I. N.	♂	8/12	28	Upper spinal	±	..	−	−	−	±	±	−	−	−	Died of acute gastro-enteritis
18	M. K.	♀	6	7	Ascending spinal	+	..	+	?	−	+	+	+	+	+	
19	E. A.	♂	32	5	Ascending spinal	+	+	−	−	+	+	++	−	−	+	
20	H. V.	♂	7/12	? 7	Ascending spinal	+	±	±	+	+	+	+++	±	+	+	Diffuse infiltration predominates

21	S. G.	♂	2 6/12	3	Upper spinal	+	+	+	?	+	+	++	+	+	+	
22	A. K	♀	4	3	Upper spinal	+	..	+	±	+	+	++	+	+	+	
23	R. C	♀	2	5	Meningitic	+	..	?	−	+	+	+	−	−	+	
24	R. S	♀	3	3	Upper spinal	+	..	+	+	+	..	..	..	..	..	Sections lost
25	S. R.	♀	1 5/12	4	Upper spinal	+	+	+	?	+	+	++	−	−	±	
26	J. S	♀	1 6/12	4	Ascending spinal	++	+	+	+	+	+	++				
27	A. K	♀	9/12	6	Meningitic	+	..	−	−	−	..	..	..	..	..	Sections lost
28	M. G	♂	9/12	34	Upper and lower spinal	+	..	−	+	+	+	++	+	+	+	Lobar pneumonia
29	G. C.	♂	1 6/12	4	Upper spinal	+	..	+	?	+	+	++	+	−	+	
30	P. C.	♂	24	6	Ascending spinal	±	..	−	−	+	±	++	−	−	−	
31	S. G.	♂	1 6/12	3	Upper spinal	..	..	+	+	+	+	++	−	−	+	
32	K. V.	♂	3	3	Ascending spinal	+	?	..	..	..	+	+++				
33	B. V.	♂	6/12	3	Upper spinal	+	+	±	−	−	+	+	−	−	−	
34	F. S.	♂	2	?	Upper spinal	+	−	−	±	−	±	+	+	+	+	Moribund on admission
35	E. P.†	♂	2/12	13	Ascending spinal	±	±	−	−	±	±	+	−	−	−	
36	I. K.	♂	27	5	Cortical	++	+	?	?	−	..	..	..	..	..	Sections lost
37	D. M.	♂	5 6/12	5	Upper spinal	+	+	+	+	−	±	+	±	±	±	
38	J. A.†	♂	4	3	Ascending spinal	+	+	−	−	+	±	+	−	−	+	
39	G. B.†	♂	58	22	Meningitic	+	..	..	..	..	+++	+	..	..	..	Partial necropsy
40	A. V.†	♂	2 2/12	3	Upper spinal	+	+	−	±	+	+	+	−	±	+	
41	W. C.‡	♂	?	?	?	..	..	..	..	..	..	++	?	?	?	Cord only was sent to laboratory
42	H. B.‡	♂	?	?	?	..	..	..	..	..	..	++	?	?	?	Cord only was sent to laboratory
43	H†	♂	9	10	Meningitic	+	+	..	..	..	+	+	..	..	..	Only cord and brain examined

* Explanatory: − = no pathologic change; ± = slight change; + = distinct change; ++ = marked pathologic change; +++ = very marked pathologic change.

† Necropsy at home. ‡ Place of necropsy unknown or none had. In all other cases necropsies at Willard Parker Hospital.

into two classes: one in which the process begins in the lumbosacral cord and progresses upward involving the arm and respiratory centers, and the other, in which the process begins in the cervical and bulbar regions or in the gray matter from which the cranial nerves have their origin. Those cases exhibiting disturbance of upper motor neuron or other disturbance of the sensorium belong to the cortical type. Those cases showing only marked meningeal symptoms were considered to be of the meningitic variety. They are as follows:

Type of Cases	Number
Ascending spinal	17
Upper spinal	18
Cortical	2
Meningitic	4

In one of the ascending spinal cases the patient survived the poliomyelitis infection and died of lobar pneumonia thirty-four days after the onset of illness. Another patient belonging to the upper spinal group, died of acute gastro-enteritis twenty-eight days after the onset of the poliomyelitis infection.

The gross changes when in the brain were chiefly those of varying grades of congestion of the pial and parenchymatous vessels; of edema of the pia and brain substance. In a few instances, the brain tissue was of softer consistency than normal. One brain, in a man of 27 years, besides intense congestion and edema, presented extreme softening in one hemisphere involving the motor area and a great portion of the parietal lobe in which lies the sensory area. Clinically, this man presented a hemiplegia and hemianesthesia of the opposite side. The brain tissue was reduced to mushy consistency with multiple hemorrhagic flecks throughout the cut surface. No gross hemorrhage was visible and the spinal fluid was clear, with changes such as one would find in poliomyelitis. The Wassermann was negative. This is the only cortical case of simulating apoplexy that came under observation at the Willard Parker Hospital among a great number of cases. The changes in the spinal cord were observed mainly on cut sections through the pons, medulla and upper cervical portion, it being our intention to preserve as much as possible of the material in a clean state for cultures, microscopic study and animal experimentation. The cut sections presented degrees of hyperemia and swelling of the gray matter. The gray "H" bulged above the level of the surrounding white matter and was sharply demarcated from same. In marked cases, the gray matter was simply pink tinged and easily marked off from surrounding white matter. Sections through normal cords fail to show the ready differentiation between gray and white matter which is to be observed in cords from poliomyelitis infection. In some cases

the edema involved the white matter as well and appeared to soften the cord as a whole.

The heart and lungs showed no striking changes, except that practically all of the lungs presented acute edema and congestion incident to the paralysis of respiration.

The liver and kidneys showed varying degrees of acute congestion, and in some cases, parenchymatous degeneration.

Particular attention was paid to the lymphatic structures, as some observers contend that lymphoid tissue plays a considerable rôle in the pathologic picture of acute poliomyelitis. The lymphoid structures of the small intestines, the Peyer's patches and solitary follicles, in a number of instances, were considerably raised and reddened. There were no indications of ulceration. The mesenteric lymph nodes were enlarged and reddened. The spleen, in many cases, showed marked congestion and more or less prominence of the malpighian bodies.

Following is a tabulation of gross changes as described in the foregoing:

	Present	Absent	Not Noted or Examined
Brain	35	5	..
Cord	20	5	15
Intestine	16	8	16
Mesenteric nodes	19	10	11
Spleen	18	16	6

A number of the necropsies were granted only for the examination of the brain and cord, and this fact accounts for the incompleteness of the data as to the other organs.

The microscopic pictures of the central nervous system in this study correspond closely with those described by Rissler, Wickman and Harbitz, and Scheel. The disease process involves all the elements that enter into the makeup of the central nervous system.

The pia mater in most cases was affected most severely in that portion which is opposed to the most severe process in the subjacent cord. Thus, in the ascending spinal type the most marked changes are to be found in the pia of the lumbosacral region, whereas in the upper spinal type the severest changes will be found in the pia of the upper cord, medulla or pons. However, quite a number of sections presented intense round cell infiltration of the cord proper, whereas the pia of the corresponding level showed little or no cell invasion. These changes consist of congestion of the blood vessels, round cell infiltration of varying degree, both around the blood vessels and also diffusely in the interstitial tissue and edema, all of which produces a thickening of the membrane. Of the thirty-nine cases, only two failed to show infiltrative changes in the pia of the cord in any of the sections studied. In six, these changes were very slight, consisting mainly of

congestion and a slight degree of perivascular infiltration. Two of these were seven and five day upper spinal cases. In the five day case, lesions were found only in the pons and medulla. In one of the remaining cases the inflammatory changes both in the pia and cord proper were slight, but the extent of nerve cell destruction was out of proportion to that of the inflammatory process. In another case, while there was only a considerable degree of congestion and edema

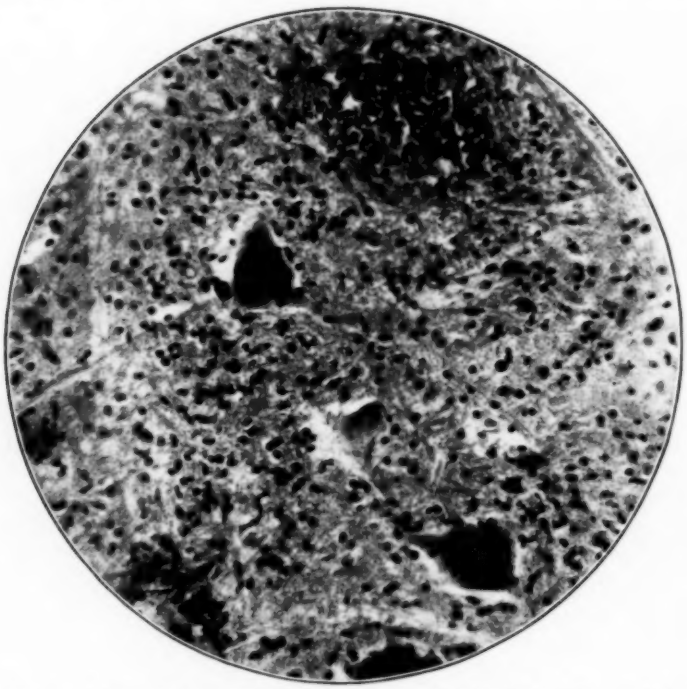

Fig. 1.—Cord showing considerable round cell infiltration. Two of three nerve cells are fairly well preserved. One of these, however, shows early phagocytosis.

of the pia without cellular infiltration, the gray matter was densely infiltrated with cells.

The pia of the brain and cord presented changes varying from simple congestion and edema to a marked degree of cellular infiltration and thickening of the membrane.

SPINAL CORD

The spinal cord presented changes of the most severe type usually in that part of its extent that was diseased as indicated clinically by the flaccid paralysis, usually in the lumbar and cervical enlargements.

These changes consist of varying degrees of perivascular infiltration; diffuse interstitial cellular infiltration of the gray matter and occasionally of the white matter; of degeneration and phagocytosis of the ganglion cells, most marked as a rule in the anterior horns, and some degree of edema. Ten of thirty-nine cases examined exhibited hemorrhage in one or both anterior horns. Cords in which hemorrhage occurred presented evidences thereof at all levels in varying degree. The gray matter was particularly affected. Ganglion cells were severely damaged. There was, however, little or no round cell infiltration. There was marked edema. The most marked ruptures occurred in the anterior horns, and in one the horn was almost completely

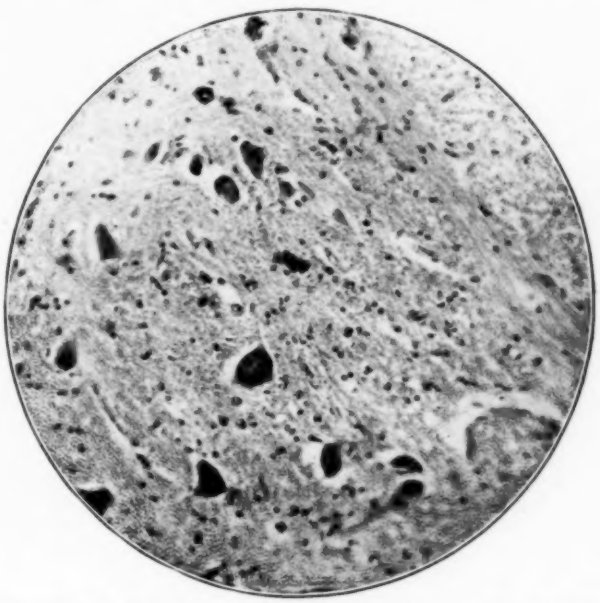

Fig. 2.—Section of cord; marked nerve cell degeneration without round cell infiltration.

destroyed by the extravasation. Fibrin deposit or other evidence of thrombosis was not noted in any of the vessels.

The perivascular infiltration is most marked as a rule about the vessels in the anterior and posterior median fissures, and in the vessels of the tips of the horns. The vessels of the horn proper seldom show a marked degree of perivascular infiltration, whereas the two vessels, one on each side of the central canal, while they exhibit extreme dilatation and congestion have not presented infiltration in any of the cases studied thus far.

The most intense diffuse infiltration is usually to be found in the anterior horns. In most of the cases studied, however, the whole of the gray matter participated, sometimes more on one side than another. In one case the posterior horn showed the greater cellular infiltration. It was noted, too, in a number of cases that where the diffuse interstitial infiltration was marked, the perivasculaar change was less marked and vice versa. In a few cases it was noted that at the lower levels of the cord the diffuse infiltration was marked and the perivascular changes not very severe, whereas at the upper levels of the same cord the perivascular infiltration was very severe while there

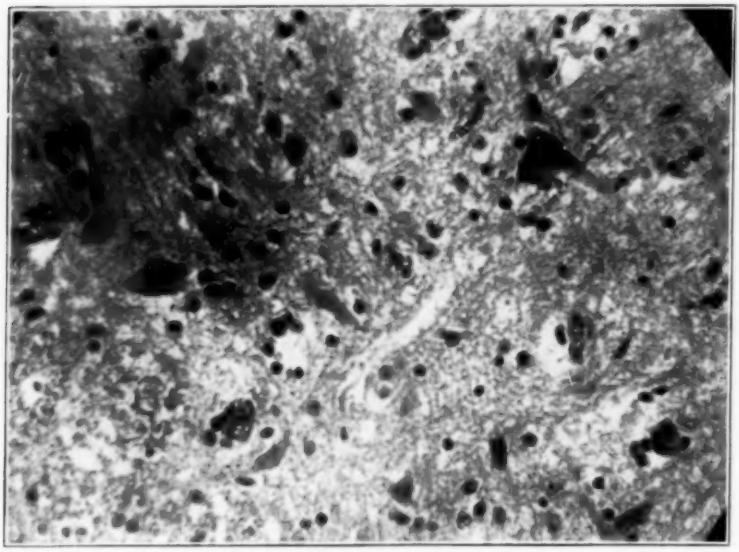

Fig. 3.—Section of cord showing considerable nerve cell degeneration with little or no cell infiltration.

was little or no diffuse interstitial infiltration. This would indicate that the perivascular infiltration precedes the diffuse cellular infiltration and that the latter is derived from the former.

The cellular exudate consists largely of mononuclear cells, with a small sprinkling of polymorphonuclear cells. In two of the cases, the polymorphonuclears were the predominating cells. The mononuclears are of two varieties; one, with a round, deep blue, evenly stained nucleus with only a scanty amount of protoplasm around it; the other, with a nucleus which may be round or ovoid, pale staining, reticulated nucleus and a moderate amount of protoplasm around it. This is the polyblast as described by Maximov. It probably represents

the first type in an active state. The nuclei of the polyblast assume odd shapes, such as the dumbbell, and the crescent. In some cells, there is a division of the nuclear material forming the polyform cells described by Flexner as being present in the spinal fluid of monkey poliomyelitis. The first type of mononuclear cell predominates in the perivascular infiltrations, whereas in the diffuse interstitial infiltrations the polyblast is the predominating cell type. This peculiar distribution can be readily explained by supposing that the cells in the perivascular infiltration are in the process of mobilization, whereas those of the interstitial tissues are in the active process of destroying the virus and

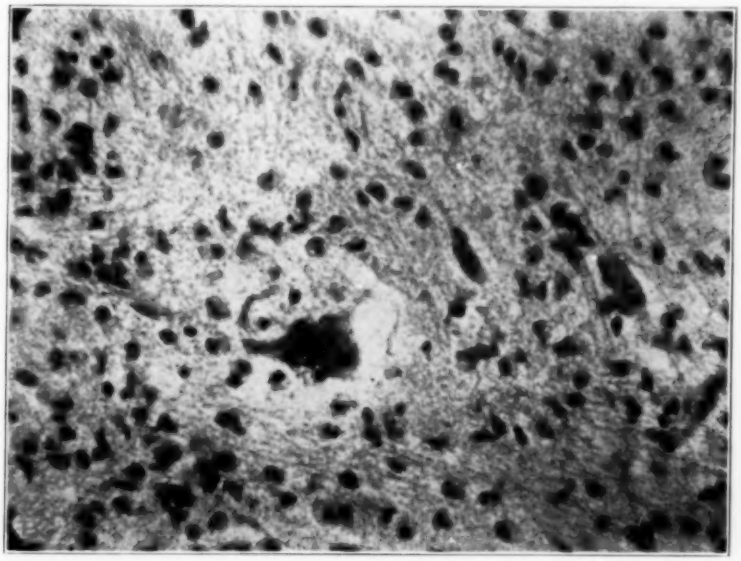

Fig. 4.—Section of cord; invasion of degenerated nerve cell by phagocytes.

carrying off destroyed nerve cells. This would account for the change of the mononuclear into the polyblast. The source of these cells is undoubtedly the lymphatic system, which discharges them into the central nervous system directly by the perivascular lymph spaces and indirectly by the blood stream. It is possible that the glia takes part in the acute infiltrative process, but it is not very probable. Certainly the glia cells of the white matter show very little activity, and if they were responsive to the invasion of the virus, it is to be expected that they would proliferate more than is evident from study of the sections. There can be no doubt as to the part the glia plays in the process of repair, but they participate little if any in the acute infiltrative process.

Infiltration of the tissues with fluid was noted as being present in the gray matter in varying degrees and in not a few instances also in the white matter. The edema appears to make the tissue more spongy and separates the reticular meshwork. As Wickman has pointed out, the recession of edema may have much to do with the rapid disappearance of paralysis that is often observed in this disease.

Destructive effects on the nerve cells were noted in all the cases, those most commonly affected being in the anterior horns. Clarke's column suffered in those cases in which the posterior horns were markedly affected. In most cases, the intensity of the nerve cell

Fig. 5.—Pia from brain showing great thickening due to edema and cellular infiltration. Blood vessels are dilated and engorged.

destruction varied directly with the degree of interstitial cell infiltration. There were many sections, however, in which the nerve cell destruction was markedly out of proportion to the degree of cellular infiltration. A number presented extreme ganglion cell destruction with practically no interstitial change. On the other hand, there were cases with marked cellular infiltration in which the cells were in fair state of preservation. These are observations that corroborate the findings of Rissler and his followers.

The changes in the nerve cell progress from the loss of the Nissl's granules to complete hyalinization, in which all nuclear material is absent. In those cases in which the cell infiltration is marked, hardly a nerve cell is to be found. Here also are to be seen polyblasts

arranged in small groups in positions formerly occupied by nerve cells. This represents complete phagocytosis. Other degenerated nerve cells are to be seen in the process of being invaded by polyblasts. In those cases in which the cellular reaction is not marked and where considerable nerve cell damage exists, there are to be seen numbers of nerve cells in the state of hyaline degeneration. On the other hand, as already stated, where there is a marked cell reaction, there are few nerve cells to be seen. This is an observation which is pertinent to the question of the rôle performed by the interstitial elements in the pathology of this disease.

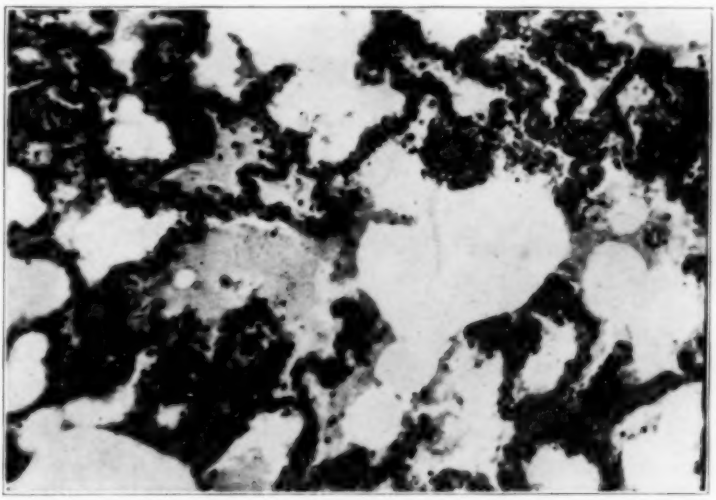

Fig. 6.—Section of lung showing thickened alveolar walls due to infiltration with small round cells.

The pons and medulla exhibited round cell infiltrations and degenerative changes in thirty of the thirty-five cases examined. The remaining five showed marked congestion of the blood vessels. In one case, the pons and medulla presented the only changes found in the central nervous system. The cell infiltrations for the most part were located in between the bundles of fibers, with no tendency to localize in any particular region. Rarely were they found in the region of the nuclei. In nine of the cases there was marked diffuse infiltration. One section presented a large hemorrhage. The nerve cell changes were not as marked as in the cord. Often one group of nerve cells exhibited degenerative changes, whereas an immediately adjacent group would appear quite normal.

The changes in the cerebrum and cerebellum were very mild when compared with those in the cord. The most common change consisted of engorgement of the vessels, the endothelium of which had the appearance of being swollen. In fourteen of thirty-seven cases the brain exhibited very mild cell reactions, consisting in slight degree of perivascular infiltration and, in a few cases, in an accumulation of cells apart from the vessels. The nerve cells exhibited no degenerative changes. The cerebellum exhibited similar changes in five of thirty-three cases examined. These changes were most commonly found below cellular layers in the cerebrum and below the granular

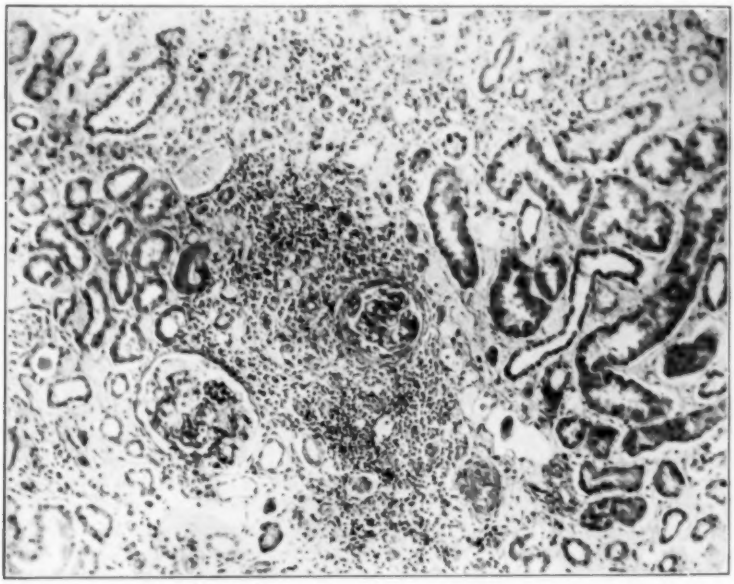

Fig. 7.—Section of kidney showing round cell infiltration and degeneration of glomeruli and tubules.

and Purkinje cell layers in the cerebellum, in among the fibers radiating from the cortex. It is unfortunate that the sections of the two cortical cases have been lost, as they would undoubtedly have presented interesting changes.

CHANGES IN OTHER ORGANS

Careful studies were made of the lymphatic structures, particularly the agminated and solitary follicles of the small intestine, the mesenteric lymph nodes and the spleen. The thymus gland was studied in a few cases. Of twenty-nine cases in which the small intestine and mesenteric nodes were examined, sixteen presented distinct changes.

In twenty-one of thirty-one cases the spleen presented similar changes. These consisted of a simple congestion of the blood vessels and distinct proliferation of the reticular cells, and marked hyperplasia of the endothelial cells. The germinating centers were increased in number and size and were very active. Moderate numbers of mitotic figures were present. The spleen in a number of instances presented intense congestion which dominated the picture. In no case was there attempt at ulceration of the intestinal mucosa over the lymphatic structures, and the adjacent mucosa failed to present cell infiltration such as one would expect in case of an active local inflammation, as in typhoid fever. In a number of cases, the lymphatic nodules adjacent to the bronchioles in the lungs exhibited changes as above described.

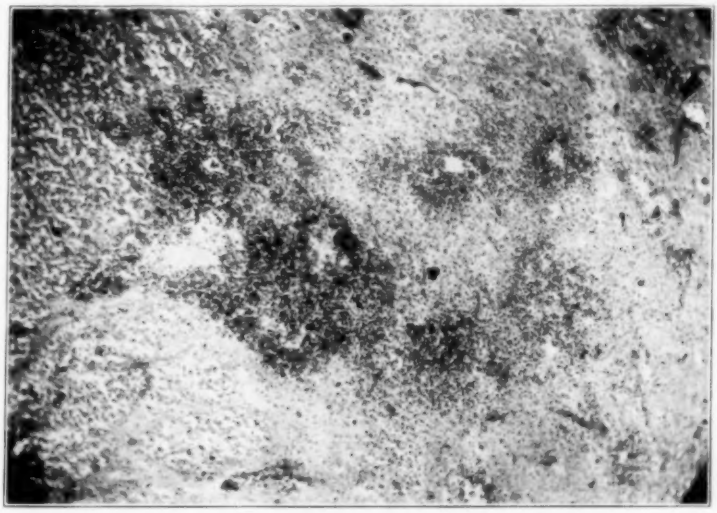

Fig. 8.—Large hemorrhage into cord.

The lung capillaries were very often intensely engorged and tortuous. In a number of cases air vesicles presented an accumulation of fluid and desquamated epithelial cells. The majority of the lung sections examined presented a marked thickening of the alveolar walls, due in part to engorgement of the capillaries, but in the main to round cell infiltration. Some of the blood vessels presented a narrow collar of these cells very much like the perivascular changes observed in the cord proper. These changes may be the pathologic basis of the so-called "paralytic râles" observed by Louria.

The heart presented congestion of the small vessels, in many of which there was evidence of hyperplasia of the endothelial cells. In some instances there was slight perivascular arrangement of mono-

nuclear cells, such as Wickman had described in the subpericardial fat. These changes were noted only about thin walled vessels in the connective tissue septa between the muscle bundles. The larger, thick walled vessels did not exhibit such changes. The muscle fibers showed no pathologic change.

The liver, in quite a number of instances, exhibited an increase in small round cells in Glisson's capsule and some of the thin walled vessels presented endothelial hyperplasia. The entire vascular system was intensely engorged in many instances. Focal necroses such as described by Flexner, Peabody and Draper, were not noted, though

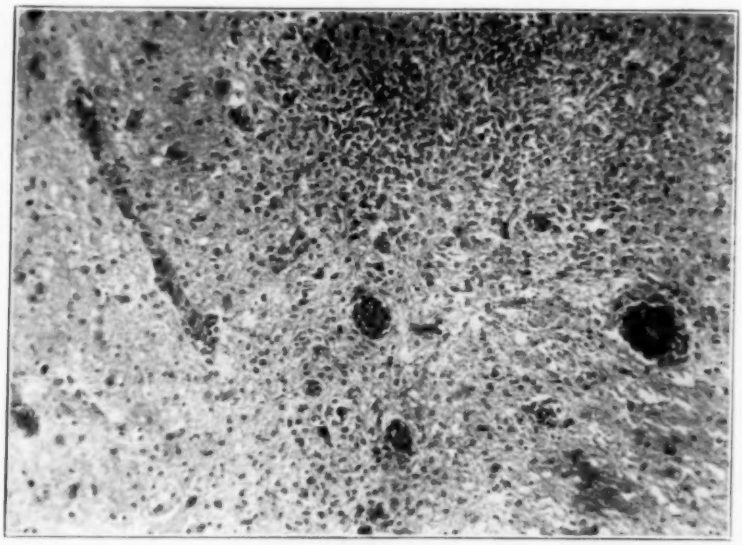

Fig. 9.—Section of cord. Marked diffuse infiltration; very slight perivascular cell infiltration.

in some cases there was marked hyaline degeneration of liver cells throughout a section and not localized in foci.

The kidneys in practically all instances were intensely engorged throughout both the cortex and medullary portion. In some cases there was to be seen hyperplasia of the endothelium of the malpighian tuft, so that it would appear as a ball of cells. These tufts appeared slightly smaller than adjacent tufts in which this hyperplasia was absent, perhaps due to the weight of the cells which prohibited the dilatation of the capillaries. Only occasionally was there evidence of parenchymatous degeneration. In two cases the kidneys presented focal accumulations of round cells, chiefly in the cortex. There was no evidence of a chronic inflammatory process such as one would

encounter in tuberculosis. The masses of round cells were disposed particularly around the glomeruli and produced degenerative changes in these, possibly by pressure. The cells infiltrated the spaces between the tubules, distorting relationship to each other and to the glomerulus. The tubular epithelium presented granular degeneration. Bowman's capsule was swollen and presented hyaline change. The capillaries were engorged. The changes presented all the characters of an acute process, except that the cell element was the mononuclear instead of the polynuclear. Whether these kidney changes are manifestations of the systemic disease is problematical. However, they are suggestive.

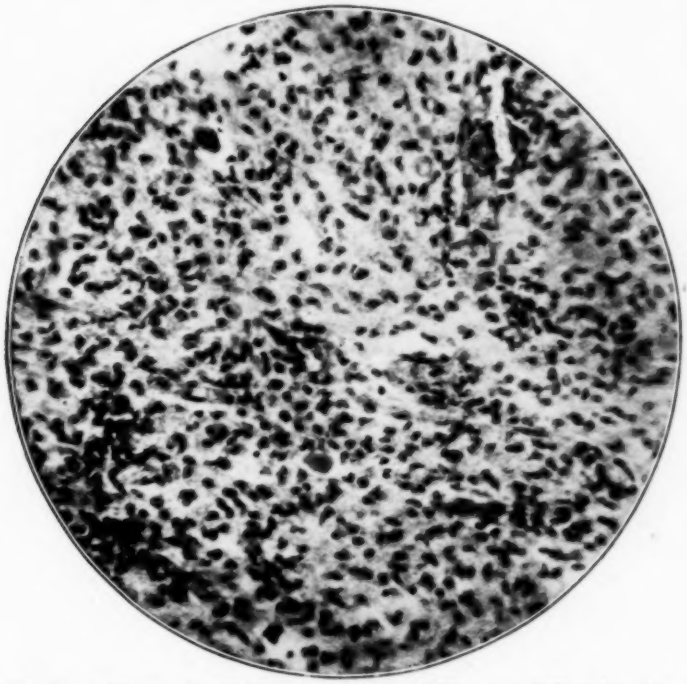

Fig. 10.—Section of cord showing intense diffuse cell infiltration but no perivascular infiltration.

The pancreas and suprarenal capsule, aside from congestion and occasionally hyperplasia of the lymphatic elements, presented little that was abnormal.

The question arises, what is the significance of the changes observed in organs other than the central nervous system? The changes in the intestine are not such as to lead one to suspect it as being the portal of entry. The changes in the lymphatic system and endothelial hyperplasia observed in the other organs are undoubtedly a general response

of the body cells to an intense local infection situated in the central nervous system. Poliomyelitis is a local infection inasmuch as the chief anatomical lesions are situated in the central nervous system, but this local condition may engender a general response, just as in pneumonia the lung is the focus and the toxemia and the defensive response are general. The changes in the organs other than the central nervous system are not of a destructive character, but rather of a defensive nature.

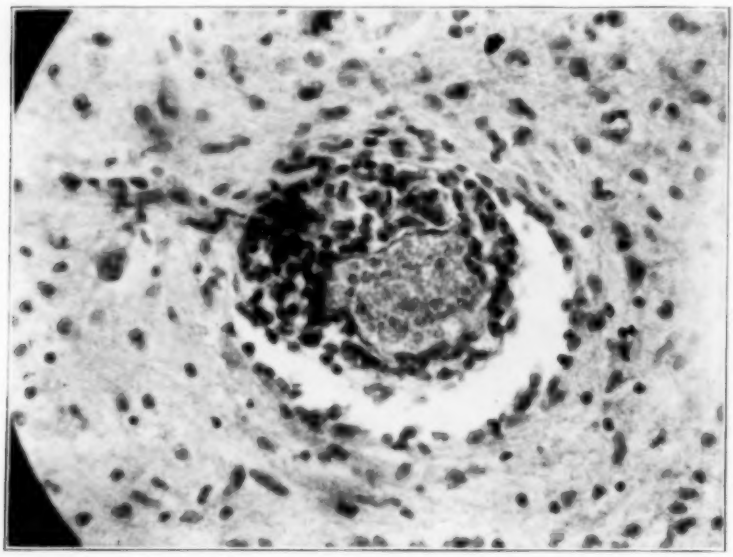

Fig. 11.—Section of cord. Perivascular cell infiltration; very little diffuse infiltration.

PATHOGENESIS

The question of pathogenesis has divided the workers in this field into two groups. One contends that the damage to the nerve cell is the primary lesion and the evidences of inflammatory changes are secondary; the other, that the inflammatory changes are the direct cause of the changes observed in the nerve cells. Charcot[10] was the first to bring forth the first view. He was supported in this view by Rissler, who was the first to describe the pathologic changes in acute poliomyelitis.

Roger and Damaschino[11] were the first to advocate the primary importance of the interstitial changes. They have received strong

10. Charcot and Jaffray: Arch. physiol. norm. et pathol., 1870.
11. Roger and Damaschino: Rev. de méd., 1881.

support from Wickman and Harbitz and Scheel, and a number of the more recent students of the disease. Wickman differs from Harbitz and Scheel in that he believes that the virus reaches the spinal cord by the way of the perineural lymphatics, whereas the latter authors contend that the path of infection is through the blood stream.

That the virus of poliomyelitis has a specific affinity for the nerve cells of the spinal cord, particularly those of the anterior horn, is indicated by the fact that no matter where the virus is introduced it reaches the spinal cord, whether by the subcutaneous, blood, intestinal, respiratory or intracerebral routes. The behavior of the virus in this respect is analogous to that of rabies. The bulk of experimental

Fig. 12.—Section of cord. Marked perivascular cell infiltration; slight diffuse infiltration.

evidence thus far adduced strongly indicates that the virus reaches the central nervous system by way of the perineural lymph channels. It has been proved that the rabic virus takes a similar path to reach the central nervous system. The majority of the workers concede that the perineural lymph route is without a doubt the path of infection. Harbitz and Scheel, however, contend that the virus reaches the pia from the blood and spreads from this site to the cord itself along the sheaths of the blood vessels. Experimental work, however, has not supported this idea.

It would appear that Wickman's ideas of the pathogenesis are somewhat inconsistent. To grant that the virus reaches the cord by

the perineural lymph channels, that the lymph which bathes the nerve cell contains the virus of poliomyelitis, and yet to consider that the nerve cell destruction is brought about by the interstitial phenomena is at variance with what is logical in such circumstances. Furthermore, Rissler, Cassierer and also the present study, present evidence which would indicate that the marked nerve cell destruction can exist with a minimum of inflammatory reaction. Kling, Petterson and Wernstedt[12] have observed changes in monkey poliomyelitis which they described as purely degenerative in character. Because interstitial changes occur in the great majority of cases along with nerve cell changes is no reason for the assumption that the former produces the latter. The fact that there is evidence, even though small in quantity, that nerve cell destruction may be present with a minimum of cell reaction, is sufficient to overbalance the fact that nerve cell destruction is so prevalent in sections showing marked cellular infiltrations. To assume that polyblasts have the power of invading healthy and intact nerve cells and destroying them, is rather far fetched. A more logical assumption would be that the nerve cells being destroyed or damaged are fit subjects for the phagocytic activities of the polyblasts. This, too, would explain why in those sections that present marked cell destruction there is a marked accumulation of polyblasts. Furthermore, it would explain why apparently healthy and intact nerve cells are present in the midst of a densely infiltrated zone without the sign of being subjected to phagocytosis. Those cases in which the interstitial change is so slight, though there is considerable evidence of nerve cell destruction, can be explained by diminished ability to react to the virus, which primarily affects the nerve cells.

The pathogenesis of acute poliomyelitis, in the opinion of the writer, is as follows:

The virus has a special affinity for nerve cells, more particularly the anterior horn cells. It reaches the central nervous system by way of the perineural lymph channels. The process spreads in the central nervous system by the lymphatics. The congestion, edema and cellular infiltration, whether present in the pia or in the cord itself, are the cardinal elements of an inflammatory reaction in response to injury produced by the activity of the virus in the cord. The neurophagocytosis is not an active primary destructive process, but rather the exercise of the known normal functions of leukocytes, that of carrying off destroyed material. The congestion and edema, undoubtedly, play a considerable part in the production of transient paralysis through pressure effects.

12. Kling, Petterson and Wernstedt: Ztschr. f. Immunitätsf., **12,** 316 and 657; **14,** 303; 1912, **16,** 17.

FURTHER OBSERVATIONS ON THE ABERRANT ELECTROCARDIOGRAM ASSOCIATED WITH SCLEROSIS OF THE ATRIOVENTRICULAR BUNDLE BRANCHES AND THEIR TERMINAL ARBORIZATIONS

CLINICAL AND HISTOLOGIC REPORT OF A CASE IN WHICH SUCH ABERRANT COMPLEXES WERE OBTAINED *

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CLEVELAND

In a previous paper[1] we reported the clinical observations on twenty-two cases in which *aberrant* electrocardiograms were obtained, attributing the abnormal type of the ventricular complex to a temporary or permanent defect in conductivity of the branches of the atrioventricular bundle.

As characterizing the essential difference between the *aberrant* electrocardiogram and the normal type, we emphasized the prolongation of the P-R interval beyond 0.20 second; the increase in the duration of the QRS interval beyond 0.10 second, particularly when it constitutes more than one third of the duration of the entire complex; the deflection of the T-wave in a direction opposite to that of the prominent initial deflections, with frequent conspicuous exaggeration of its amplitude; the relatively increased amplitude of the initial deflections of the ventricular complex in an opposite direction in Leads I and III, often markedly notched, and finally, the tendency of these deflections to assume a diphasic rather than a triphasic or quadriphasic type.

In this earlier report, based wholly on material collected in Dr. Lewis' laboratory in London, no attempt was made to discuss the nature of the histologic changes in any of the cases of this series that came to necropsy. The evidence for our conclusions as to the nature of the defect in conductivity was apparently well established by the *then* available experimental work of Eppinger and Rothberger,[2] by the observations of Eppinger and Stoerk[3] who had, in two cases, con-

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* From the Medical Clinic of the Cleveland City Hospital and the Western Reserve University.

1. THE ARCHIVES INT. MED., 1914, **13,** 803.
2. Eppinger and Rothberger: Ztschr. f. klin. Med., 1910, **70,** 1.
3. Eppinger and Stoerk: Ztschr. f. klin. Med., 1910, **71,** 157.

firmed by a histologic examination the clinical diagnosis, made from the electrocardiogram, of a lesion of the right branch of the atrioventricular bundle, and by the case reported by Cohn and Lewis[4] of atrial fibrillation and heart block, in which the histologic examination showed a destruction of both branches of the atrioventricular bundle, the electrocardiograms obtained from this case being practically identical with the curves obtained from a *similar experimental* lesion by Eppinger and Rothberger.

In a previous report of four cases characterized by abnormal electrocardiograms, Mathewson[5] asserted that "in the present state of our

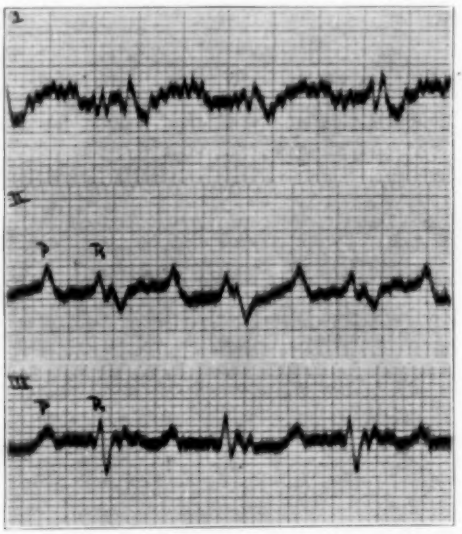

Fig. 1.—March 21, 1916. The P-R interval measures 0.24 second. The QRS measures 0.16 second. The T-wave is inconspicuous, especially in Lead II. It is upright in Lead I and inverted in Lead III. The QRS complex shows more than a simple notching, having a distinct triphasic character. It cannot be said that the conspicuous initial ventricular deflections are in a direction opposite to each other in Leads I and III. Their voltage as expressed by amplitude is low. This record taken on admission to the hospital *before* digitalis was given.

In this and the succeeding figures 1 scale of divisions of ordinates equals 10^{-4} volts; 1 scale of the abscissae equals 0.04 second.

knowledge, the alterations in the electrocardiographic curves may be regarded as indicating interference with the normal stimulus conduction in the branches of the bundle."

4. Cohn and Lewis: Heart, 1912, **4**, 15.
5. Mathewson: Heart, 1913, **4**, 385.

Since the publication of our earlier series we have learned[6] that four of the hearts included in this report did not show, on histologic study of the material available, any evidence of definite lesions of either branch of the atrioventricular bundle.

In a recent paper Oppenheimer and Rothschild[7] report a study of sixty-two cases characterized by abnormal electrocardiograms, together with the results of a detailed histologic study of eleven of the hearts obtained from the fourteen necropsies in the twenty-five known fatal cases of their series. Thirteen of these hearts showed a widely disseminated patchy sclerosis of the myocardium, predominating in the endocardial and subendocardial layers, these changes being grossly

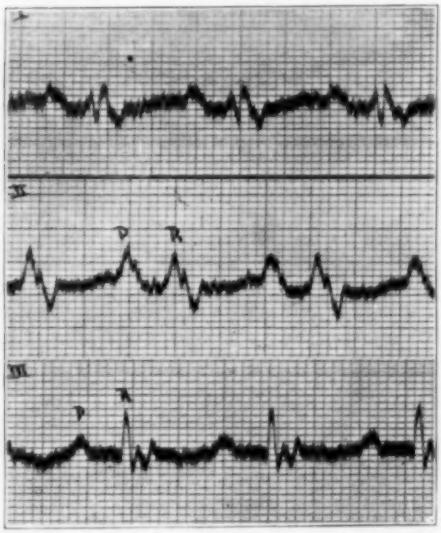

Fig. 2.—May 10, 1916. The P-R interval measures 0.24 second. The QRS interval measures 0.16 second. The T-wave is still inconspicuous. In Lead I the P-wave is to be made out. The conspicuous initial ventricular deflections are triphasic in Leads I and III, and of relatively low amplitude. In Lead II the notch comes on the descent of R almost at the iso-electric level. In Lead III R is conspicuous with a notched peak and is followed by a curiously split complex. After digitalis.

more marked in the left than in the right ventricle. Eight hearts showed also coronary artery sclerosis with occlusion of the anterior descending branch of the left coronary, while four showed nodular sclerosis of the coronary arteries with no occlusion.

6. Personal communication.
7. Oppenheimer and Rothschild: Jour. Am. Med. Assn., 1917, **69**, 429.

These observers further emphasize as the criteria for determining the abnormal electrocardiogram the prolongation of the QRS complex beyond 0.10 second, the notching of R, and call attention to the low voltage, as expressed by the low amplitude of the deflections in all three leads and the absence of the typical diphasic curves with large T'-waves seen in experimental bundle lesions. Referring to the earlier series of cases reported by the writer they say that they regard most of them as cases similar to those they describe, and call attention to the existing discrepancy between previous electrocardiographic interpretation and the pathologic findings.

In the light of our present knowledge of the occurrence of widely scattered foci of sclerosis involving chiefly the terminal fibers of the

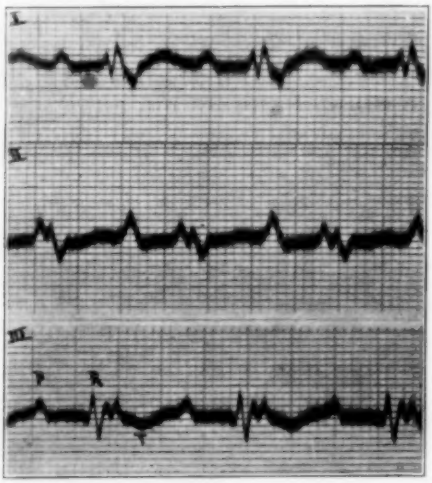

Fig. 3.—Oct. 29, 1916. On readmission. The P-R interval measures 0.26 second. The QRS interval measures 0.16 second. The T-wave is slightly more conspicuous and in a direction opposite to the conspicuous initial ventricular deflections. The QRS complex shows the same bizarre type of triphasic character, this being especially marked in Leads I and III. Before digitalis.

conduction system and giving rise to a conspicuously altered QRS complex, it is apparent that we must revise our clinical interpretation of the aberrant electrocardiogram.

In a study of a fairly large series of cases throughout the past two years we have been impressed by the frequent occurrence of aberrant electrocardiograms characterized by curves of low amplitude in all three leads and an absence of the large diphasic curves so closely simulating the experimental bundle lesion. In some instances we have been astonished by the occurrence of curves of low amplitude alternat-

ing with curves of high amplitude in the same individual, occasionally seen at but short intervals of time. We have also been impressed by the frequent occurrence of prolongation of the QRS complex with bizarre notching, and the constancy of the opposite direction of the initial deflections in Leads I and III, in the absence of any increase in the P-R interval; and by the observation that the QRS complex, although prolonged, does not in many instances, at least, attain a duration of one-third of the entire ventricular complex.

The final deflection T′ appears, however, remarkably constant in its direction opposite to that of the conspicuous initial deflections in

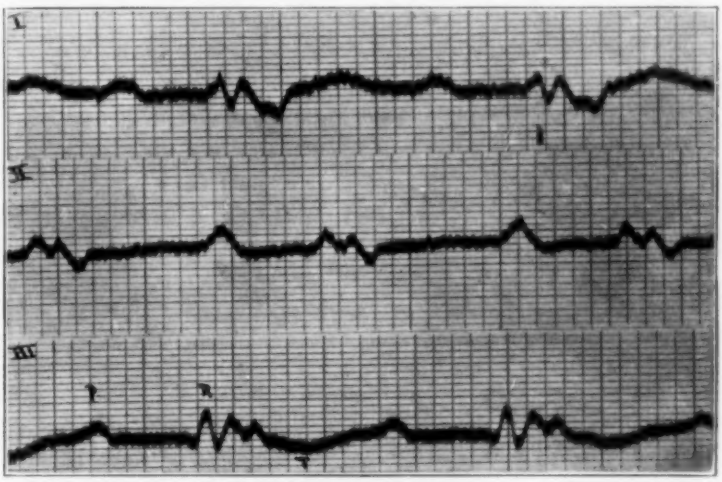

Fig. 4.—Oct. 29, 1916. In order to bring out the essential features of the electrocardiogram this record was taken with the plate dropping at a speed of 6.8 cm. per second. The low amplitude and the bizarre type of the ventricular complex are plainly seen in all three leads. Before digitalis.

Leads I and III, being inverted in Lead I and upright in Lead III, with the single exception of case 299 in our series. In case 248, cited later, this inversion is, of course, reversed during the paroxysmal attack, appearing in a direction opposite to that of the conspicuous initial deflections both during the presence of the *normal* and the *abnormal* mechanism.

What is most interesting is the fact that we have seen but a single instance simulating the experimental curves of a left bundle lesion, such as ilustrated Case 13 of our earlier series, and this only during an attack of paroxysmal tachycardia (Case 248, Fig. 7).

These points are clearly shown in the accompanying Table, in which we have grouped in tabular form thirteen cases showing conspicuous aberrant electrocardiograms taken from the last 108 of our serial cases.

There are but two cases of this series which merit any detailed discussion. The chief points of the aberrant electrocardiogram that we wish to emphasize and which are brought out by the case reported herewith in detail, and not included in this table, are seen at a glance.

TABLE 1.—Cases Showing Conspicuous Aberrant Electrocardiograms

Serial No.	Duration of P-R Interval*	Duration of QRS Complex	Duration of Total Ventricular Complex	Notching of R and S	Direction of Initial Deflections in Leads I and III	Direction of T^v in Relation to Initial Deflections in Leads I and III	Voltage as Expressed by Amplitude 1 Ordinate $= 10^{-4}$
217	....	0.10	0.18	Notched	Opposite	Opposite	Low
237	....	0.10	0.32	Notched	Opposite	Opposite	Low
255	....	0.10	0.30	Notched	Opposlite	Opposte	Low
248 During tachycardia	....	0.16	0.20	Notched	Opposite	Opposite	Very high
With normal mechanism	0.19	0.07	0.32	None	Opposite	Opposite	Normal
279	0.17	0.12	0.36	Notched	Opposite	Opposite	High
282	....	0.08	0.28	Notched	Opposite	Opposite	Low
286	....	0.09	0.32	Notched	Opposite	Opposite	Low
294	....	0.11	0.28	Notched	Opposite	Opposite	Normal
299	0.19	0.11	0.32	Notched	Opposite	Same	Low
306	0.19	0.10	0.36	Notched	Opposite	Opposite	Low
311	....	0.08	0.34	Notched	Opposite	Opposite	Low
324	....	0.11	0.36	Notched	Same	Opposite	Low
325a	....	0.14	0.48	Notched	Opposite	Opposite	Very high
325b	....	0.12	0.46	Notched	Opposite	Opposite	Low

* The P-R interval is given in those instances only in which it measured at least 0.17 second or more.

Case 248 was remarkable in that during the attack of paroxysmal tachycardia the general type of the electrocardiogram was so conspicuously altered. During the normal mechanism the conspicuous initial deflections were in opposite directions, being upright in Lead I and inverted in Lead III, and the final deflection T appeared in an opposite direction in both leads. In Lead II the ventricular complex appears normal, lacking wholly any evidence of its bizarre character which appeared during the paroxysm. The P-R interval is increased, measuring 0.19 second. The inversion of the P-wave in Lead III, Figure 6, we are at a loss to account for. It is not altogether easy to

assume that this is an expression of a change of focus for the pacemaker in this lead, when in the presence of a definitely altered focus we get the anomalous complex noted below.

We have noted a similar inversion of the P-wave in a number of instances, both in the normal individual and in pathologic cases, quite constantly occurring in Lead III, and not accompanied by any conspicuous shortening of the P-R interval. Lewis, Meakins and White[8]

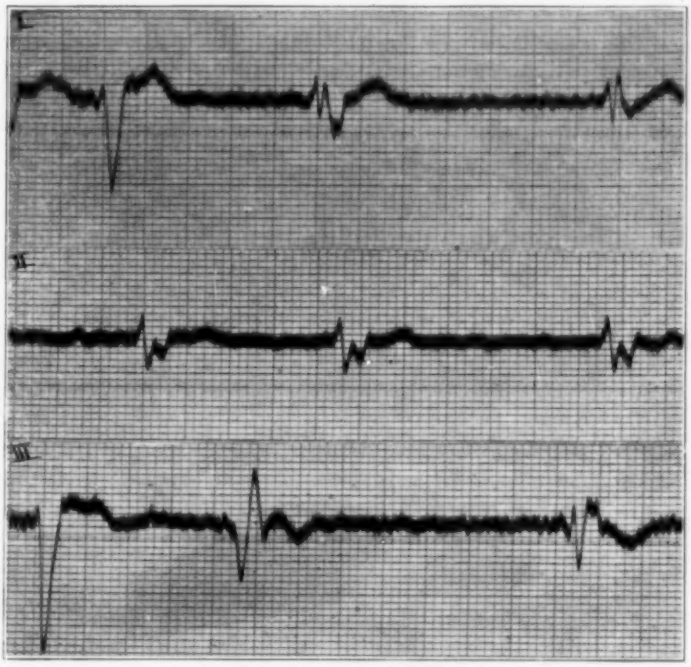

Fig. 5.—Feb. 3, 1917. After the onset of atrial fibrillation. The anomalous ventricular complex is more marked. The normal ventricular sequence is disturbed by premature beats arising from the left ventricle and junctional (?) tissue. Note the slightly increased amplitude of the initial ventricular deflections in this figure. The T-wave has increased in amplitude above the previous figures and can be distinctly made out. There has been, however, no reversal of its negativity. Digitalis was given to the point of marked slowing with digitalis coupling.

in their experimental observations on the excitatory process in the dog's heart, have recorded a shifting of the pacemaker *within* the S-A node as a result of vagal stimulation with such inversion.

8. Lewis, Meakins and White: Phil. Tr. Roy. Soc., London, Serics B, 1914, **205,** 375.

Wilson,[9] in a paper calling attention to changes in the location of the cardiac pacemaker associated with respiration, has divided these changes into three classes: (1) migration of the pacemaker within the sinus node, or within its immediate neighborhood; (2) migration of the pacemaker from the sinus node to the a-v node; and (3) escape of the idioventricular rhythm with complete atrioventricular dissociation, during which the ventricles contracted more rapidly than the auricles.

In a recent very interesting paper on heart block, Wilson and Robinson[10] in describing similar changes in the P-wave advance the view that these alterations are analogous to the change which may occur in the experimental animal under vagal stimulation.

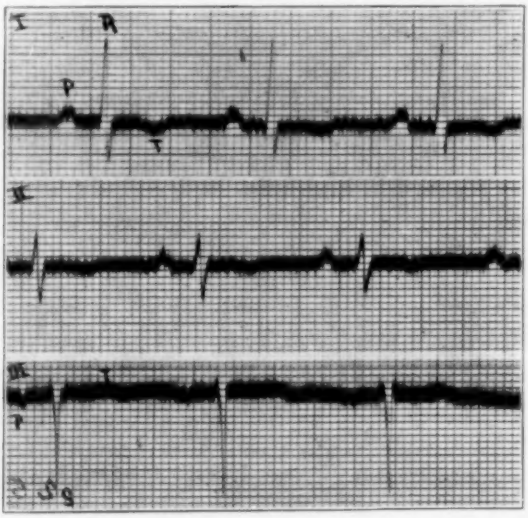

Fig. 6.—Same case as Figure 7. During the presence of the normal mechanism. There is absolutely no suggestion of the abnormal complex seen during the tachycardia. In Lead III the P-wave is inverted.

In our own observations we have been able to classify this inversion of the P-wave, seen so constantly in Lead III, into essentially two groups: one in which it is definitely under vagus control and becomes upright under atropin, and one in which vagus control is apparently in abeyance, neither atropin nor vagus stimulation having any effect on the inversion.

During the paroxysmal tachycardia in this instance the whole type of the ventricular complex was altered, being characterized by curves

9. Wilson, F. N.: The Archives Int. Med., 1915, **16,** 86.
10. Wilson and Robinson: The Archives Int. Med., 1918, **21,** 166.

of high amplitude essentially diphasic, which fact considered alone is not, of course, unusual, but when considered in the light of the direction of the conspicuous initial deflections, with the suggested notching of R′ and S′ in Leads I and III, the conspicuously altered complex in Lead II, and the great increase in the QRS complex is significant (Fig. 7).

These curves, obtained during the tachycardia, represent the single instance which has come under our observation in which the electro-

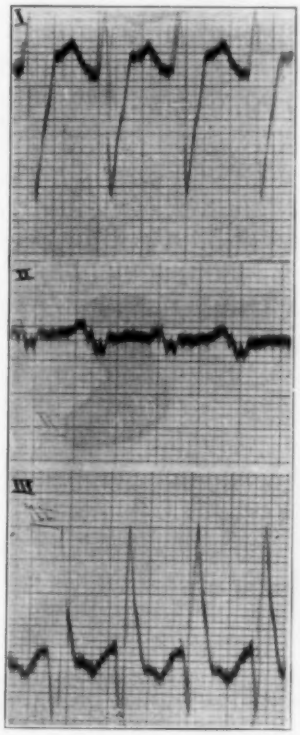

Fig. 7.—Illustrating Case 248 during the attack of paroxysmal tachycardia. Note the direction of the conspicuous initial deflections, with notching, in Leads I and III, and the anomalous complex in Lead II. Ventricular rate 180.

cardiogram showed diphasic curves of large amplitude with a conspicuous S′ in Lead I and R′ in Lead III, and a marked prolongation of the QRS complex, in so far simulating the curves obtained from experimental lesion of the *left* branch of the atrioventricular bundle.

As illustrating the occurrence of curves of high amplitude alternating with those of low amplitude, Case 325 is a striking example.

In this case the electrocardiogram obtained on admission showed, in the presence of a complete atrioventricular dissociation, typically diphasic curves of large amplitude, remarkably similar to the published experimental curves of Eppinger and Rotchberger following section of the right atrioventricular bundle branch in the dog (Fig. 8). Twenty-four hours later the large diphasic curves had disappeared and given place to an entirely different type of ventricular complex characterized

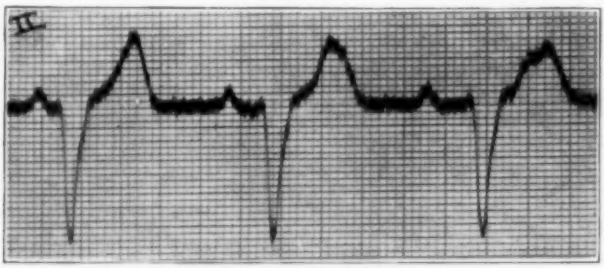

Fig. 8.—Illustrating Case 325. Record taken on admission to the hospital. Complete A-V dissociation. Lead II. Note the greatly increased amplitude of the ventricular complex and its diphasic character. S′ shows suggestive notching. The QRS interval measures 0.12 second.

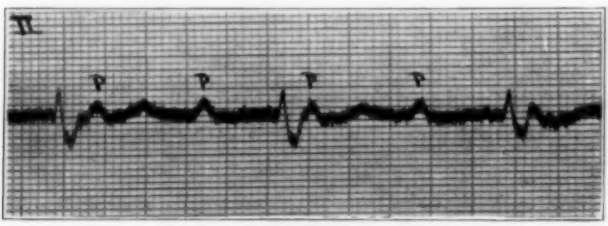

Fig. 9.—Illustrating Case 325. Twenty-four hours after Figure 8 had been taken. Lead II. Note the low amplitude of the ventricular complex with marked notching of S′. The QRS interval measures 0.12 second.

by curves of low voltage, as expressed by amplitude, with a slightly shorter QRS complex (Fig. 9).

How shall we interpret such widely divergent types of curves obtained in so short an interval of time? In the earlier curves the initial deflections have a value expressed in microvolts of 3,200 (32×10^{-4}), while later their value is but 900 micro volts (9×10^{-4}). Are we justified in assuming that the earlier records were obtained at a time when there existed a definite but temporary failure of con-

duction in the right bundle branch, which altered the *assumed* dominant type of the electrocardiogram as shown by the later curves? Based on the experimental evidence available, no other interpretation seems quite logical.

In the thirteen cases tabulated we have expressed the range of voltage, as illustrated by the amplitude of the initial deflections, as low, normal, high and very high, assuming that the so-called "normal" taken by itself is but an average standard, subject to considerable variation, but that in the presence of advanced myocardial disease the values "low" and "high" have a definite pathologic significance.

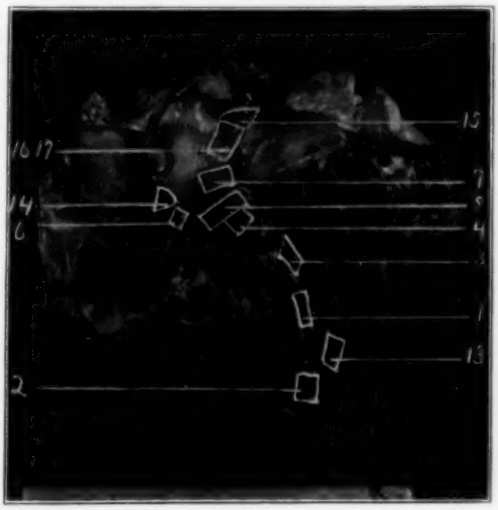

Fig. 10.—Right side of heart opened to show right atrium and ventricle, and areas of tissue blocks removed.

It will be seen that out of these thirteen cases, with the exception of Case 248, which showed a typically *aberrant* electrocardiogram only during the paroxysm of tachycardia, and Case 325, in which the earlier curves simulated the experimental bundle lesion, but one, Case 279, fulfilled the essential requirements for the diagnosis of a definite bundle branch lesion, being characterized by curves of large amplitude typically diphasic. All the other cases conform essentially to the type of curve illustrating the case we are reporting in detail, though lacking the conspicuous triphasic character of the ventricular complex so constant a feature of this case.

It will be further noted that three of the cases included in this

table did not show an increase in the duration of the QRS complex beyond 0.10 second. In so far as the prolongation of this complex constitutes a vital criterion for determining the presence of marked sclerosis throughout the conduction system, these cases should possibly be excluded. On the other hand, the electrocardiographic records obtained from these cases were in every other respect so typical of the general type under discussion that we have included them.

DETAILED REPORT OF CASE

It is greatly to be regretted that in many instances in our series we have been unable to secure a necropsy. In the case the subject of this

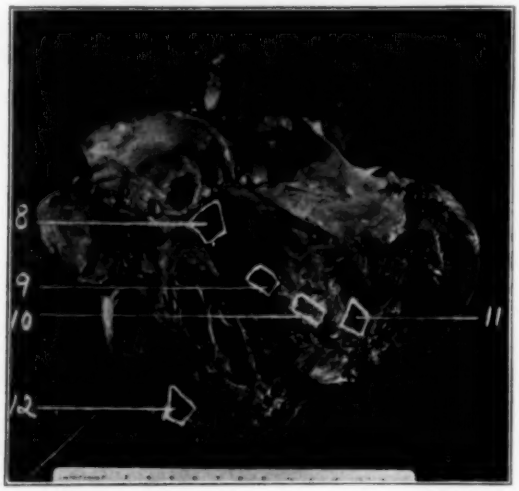

Fig. 11.—Left side of heart opened to show areas of tissue blocks removed.

note the heart was removed immediately after death and taken at once to Professor Van der Stricht[11] to whom we are indebted for the histologic study and report.

Clinical History.—Clinical Diagnosis.—Syphilitic myocarditis and aortitis; cardiac hypertrophy; atrial fibrillation; chronic nephritis and emphysema; cardiac failure and death.

The patient, S. S., a laborer, aged 42, was admitted to the City Hospital, Jan. 1, 1915, complaining of cough, shortness of breath on exertion and swelling of the feet. The family history was negative.

11. The writer wishes to express his great indebtness to Prof. O. Van der Stricht of the University of Ghent, now at the Johns Hopkins University, for his elaborate and detailed study of the heart from this case.

Personal History.—Typhoid fever at 24; pneumonia at 25. The patient says that in 1910 he had "rheumatism" in his right leg. No history could be obtained of acute rheumatic fever, and no history of any joint involvement associated with this so-called "rheumatism." He was not confined to bed at this time. He admits the history of a venereal lesion in 1900. He had had a specific urethritis several times. Used alcohol to excess up to 1912. Had had four breakdowns similar to the present attack, characterized by shortness of breath on exertion and some swelling of the feet, the first in 1910, the last in 1914.

Present Illness.—The present acute onset of symptoms dated from Jan. 1, 1915, when following a sudden overexertion lifting heavy baggage he became short of breath on the slightest exertion. This distress in breathing was soon followed by swelling of his feet and legs. He walked into the hospital.

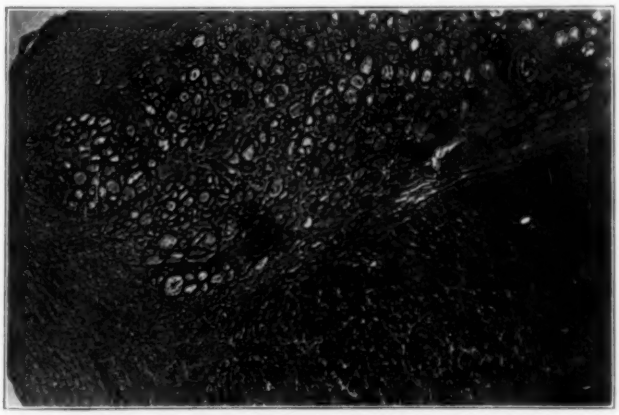

Fig. 12.—Transverse section through the left posterior ventricular branch of the bundle in the septal wall (Piece 9). Magnification 85 diameters. Showing infiltration and the extreme degree of fibrosis present in and around the bundle.

Condition on Admission.—The patient was a well developed and well nourished colored man. He was very dyspneic and coughed a good deal. The head showed no exostoses or protuberances. The ears were negative. There was no mastoid tenderness. The pupils were equal, reacted very sluggishly to light, but readily to accommodation. There was no nystagmus, strabismus or ptosis. The teeth were very poor; many badly carious molars; pyorrhea was present; tongue coated.

There was no enlargement or tenderness of the palpable lymphatic glands.

There were no deformities of the spine or long bones, and no thickening of the periosteum or of any of the joints.

Thorax: This was well formed; anteroposterior diameter increased; subcostal angle margins flared equally on inspiration; no prominence of supraclavicular fossae. The percussion note was resonant throughout, but slightly higher pitched over the right apex posteriorly. The breath sounds were everywhere vesicular in character, expiration being prolonged. At both bases

posteriorly and in the left scapular region medium moist râles were heard at the end of inspiration and beginning of expiration. Tactile fremitus was present throughout, with normal variations.

Heart: There was well marked precordial activity over a wide area. The point of maximum impulse was in the sixth interspace 16.5 cm. from the midsternal line; apex impulse forcible; diastolic impact palpable over the base in the third interspace; no thrills or reduplications palpable. The upper border of cardiac dulness was in the second interspace extending 8 cm. to the left and 3 cm. to the right; in the third interspace dulness extended 13.5 cm. to the left and 3.5 to the right, in the fourth interspace, 15 cm. to the left and 5 cm. to the right; in the fifth interspace 15.5 cm. to the left and 8 cm. to the right, and in the sixth interspace 16 cm. to the left, and to the right was merged in hepatic flatness. These measurements are from the midsternal line. No murmurs or friction rubs were heard. The first sound at the apex had a booming quality; the second sound at the base was accentuated, with a slightly tympanitic quality.

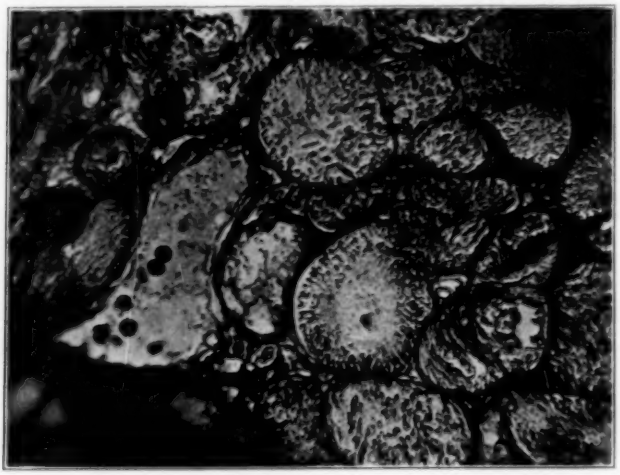

Fig. 13.—Transverse section through the left posterior ventricular branch of the bundle in the septal wall (Piece 9). Magnification 535 diameters. Showing the conspicuous cleavage of the Purkinje fibers.

The pulse rate was 96 to the minute, regular, of equal volume and synchronous in both radials. The systolic pressure was 120, diastolic 90.

Liver and spleen were not palpable.

Abdomen: No free fluid; abdominal muscles of good tone; no general or localized tenderness.

There was edema of both legs and ankles and complete right inguinal hernia.

Reflexes: Biceps and triceps reflexes equal and active; patellar and Achilles reflexes could not be elicited; normal plantar reflex.

Urine: The specific gravity varied from 1.010 to 1.018; albumin from a trace to an excessive amount was constantly present; microscopically, hyaline and granular casts were present.

The temperature remained practically normal throughout the period of observation. The Wassermann reaction was strongly positive.

The patient remained in the hospital at this time about four months, making only a fair recovery, but was able to undergo a successful surgical operation for the inguinal hernia, and was discharged June 26, 1915. No electrocardiographic records were obtained at this time as our galvanometer was not yet installed.

Readmitted March 21, 1916, with marked symptoms of failure of cardiac reserve. Extreme dyspnea, edema of legs and free fluid in the abdomen.

Heart: Marked precordial activity over a wide area; upper border of cardiac dulness at second interspace; point of maximum impulse in fourth interspace 17 cm. from midsternal line; left border of cardiac dulness 18 cm. from midsternal line in sixth interspace; right border 5.5 cm. from midsternal line in fifth interspace; sounds distant; at apex first sound was booming in character; second sound was sharply accentuated; the second pulmonic being louder than the second aortic; no murmurs could be made out; pulse rapid, regular; of moderate volume; tension increased.

Fig. 14.—Transverse section of the right atrioventricular junction, A-V node (Piece 5). Magnification 45 diameters. Showing the extraordinary degree of fibrosis of the main stem of the bundle.

At this time the patient was under observation until June 23, 1916, when he left the hospital at his own request in fair condition. The first electrocardiographic records were obtained during this period. (See discussion of figures.)

Readmitted again Oct. 23, 1916. He said that he had only been able to do the slightest work since his discharge. Ten days previously the shortness of breath and swelling of the feet became so severe that he was compelled to seek hospital care.

His condition at this time was one of great discomfort, owing to the extreme dyspnea and edema. His extremities were so swollen that he walked with great difficulty. The liver was greatly enlarged and there was free fluid in the abdomen.

Course in the Hospital.—From this time until his death he remained under observation. He showed still a certain power of response to rest and treatment, but his heart was unable to recover to anything like the extent noted on previous admissions.

The cardiac dulness was as already noted, with a marked increase in the area of dulness to the left and to the right over the aortic area. At this time a soft systolic murmur was noted at the apex on admission, but disappeared, to return again later, though never pronounced. It was regarded as a relative mitral insufficiency.

His cardiac mechanism remained normal up to Dec. 15, 1916, when atrial fibrillation developed. His blood pressure remained at or about 120 to 130 systolic and 80 to 90 diastolic up to the onset of fibrillation. The urine contained albumin in excess and many hyaline and granular casts. Death ensued Feb. 10, 1917.

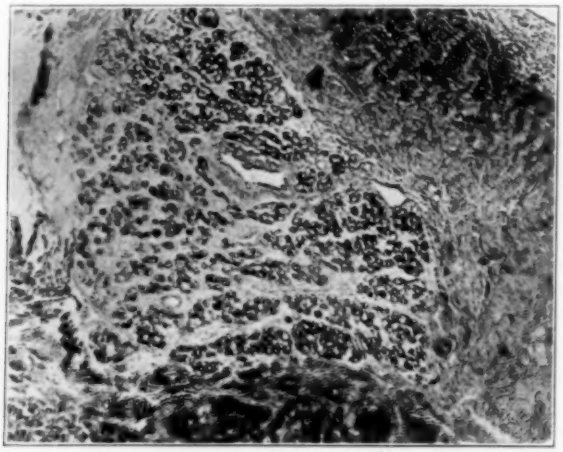

Fig. 15.—Transverse section of the stem of the bundle under the endocardium of the right ventricle beneath the septal cusp of the tricuspid valve (Piece 4). Magnification 103 diameters. Showing the great amount of fibrosis and cicatrization present.

DISCUSSION OF ELECTROCARDIOGRAMS

In selecting the figures for reproduction in this report we have chosen from a large series a number of records taken at fairly wide intervals of time, which represent the dominant type of electrocardiogram obtained throughout the period of observation, and illustrate clearly the abnormal ventricular complex so striking a feature of this case.

Voltage of Cardiogram as Expressed by Amplitude.—The high voltage as expressed by the amplitude of the P-wave, and the low voltage of the ventricular complex are at once apparent. Up to the time of the onset of atrial fibrillation the average value of the P-wave

expressed in microvolts remained practically constant in all three leads, 400 microvolts in Lead II and from 100 to 200 in Leads I and III, respectively. The amplitude of the ventricular complex, though never marked, showed a gradual increase towards the end, particularly in Leads I and III. In Lead II it ranged from 600 microvolts (Fig. 4) to 1,000 microvolts (Fig. 2). In Leads I and III the amplitude of the ventricular complex was constantly as great as, or greater than, that seen in Lead II, attaining in Figure 5 a value of 1,700 microvolts.

More interesting is the low value of the T-wave seen early, and its slight though distinct increase in the later stages following digitalis, when it reached a value of 300 microvolts. Although showing an increase in amplitude, at no time was there any reversal of its negativity.

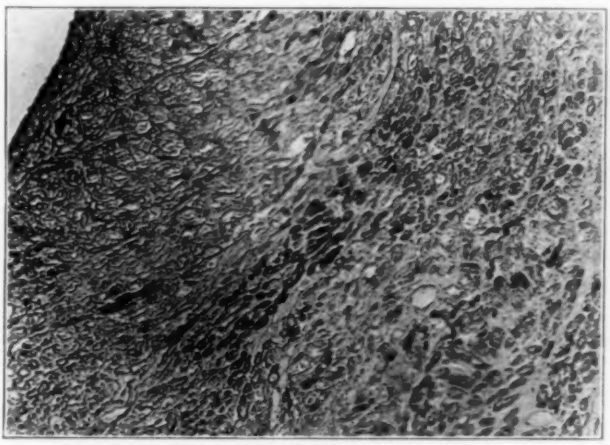

Fig. 16.—Section of the wall of the right atrium from block of tissue taken immediately above and including the margin of the coronary sinus (Piece 6). Magnification 103 diameters. To show the fibrosis of the atrial wall. The Purkinje fibers appear larger and are stained lighter than the cardiac fibers.

The QRS Complex.—The type of the QRS deflections of the ventricular complex remained constant throughout, only tending to increase the distinctness of their triphasic character as the disease progressed. The duration of the QRS interval remained constant at 0.16 second, with the exception of the measurement in Lead II (Fig. 4) where it is but 0.14 second.

The conspicuous notching of this complex seen as an interruption in the return to the iso-electric line in Figures 1 and 2, appears as a distinct alteration in negativity in Figures 3 and 4, especially marked in the latter figure, in which the plate moved at a greater speed. So

distinct was this evidence that we were inclined to assume that there might be a definite sequence in the contraction of the right and left ventricles. Keeping this possibility in mind we sought constantly for a reduplication or doubling of the first sound of the heart, hoping to obtain at least some clinical evidence of an asynchronous systole, but with negative results, as no such doubling was noted. We must not forget, however, that the electrical complex represents the propagation of the excitation wave, a change in electrical potentiality, and not a muscular action.

The T-Wave.—The amplitude of the T-wave, never marked, increased distinctly, attaining a value of 300 microvolts (Fig. 5, Leads I and III). These negatives were taken after a prolonged course of digitalis, which, however, did not alter the P-R interval, nor the direction of the T-wave. In Lead II this wave remained practically isoelectric.

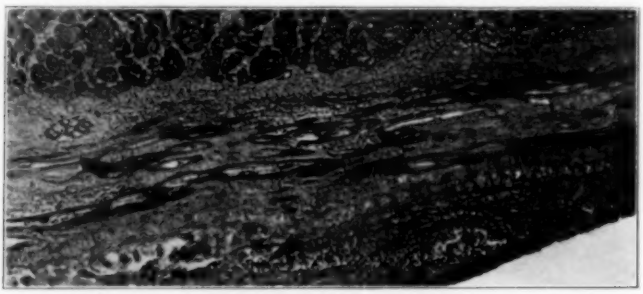

Fig. 17.—Longitudinal section of the left posterior branch of the atrioventricular bundle just below the right coronary cusp of the aortic valve. At this site the bundle first appears under the endocardium of the left ventricle (Piece 8). Magnification 103 diameters. The extent of the fibrosis in and around the bundle is plainly evident.

The failure to obtain any increase in the P-R interval or alteration in the negativity of the T-wave is in line with our results in a number of observations which it is hoped to make the subject of a future report. Using a standardized preparation, we have found, as have other observers, a striking dissimilarity in the response to the drug.

Relation of the Electrocardiogram to the Cardiac Hypertrophy.—In the light of our knowledge of the relationship of the electrocardiogram to the predominance of hypertrophy of one or the other ventricles, as shown by Lewis[12] and by Cotton,[13] our curves gave no clue to the preponderating muscle mass present in this case in the left ven-

12. Lewis: Heart, 1914, **5**, 367.
13. Cotton: Heart, 1917, **6**, 217.

tricle. It is, to be sure, true that we were dealing with a heart clinically greatly enlarged in all directions, but the striking post-mortem feature was the great increase in the mass of the left ventricle as compared with the right, which was essentially dilated. It is perhaps justifiable to assume that the normal course of the current of action was so interfered with by the diffuse sclerosis present throughout the conduction system, especially in the left ventricle, that the usual electrical complex so typical of a conpsicuous unilateral ventricular hypertrophy was annulled.

PATHOLOGIC REPORT

Heart: The heart is greatly enlarged; weight, 770 gm. The length from the root of the pulmonary artery to the apex is 125 mm. The amount of fat is not increased. There are large "milk spots" on both ventricles. The pericardium is normal. The right and left atria are large and their walls thick,

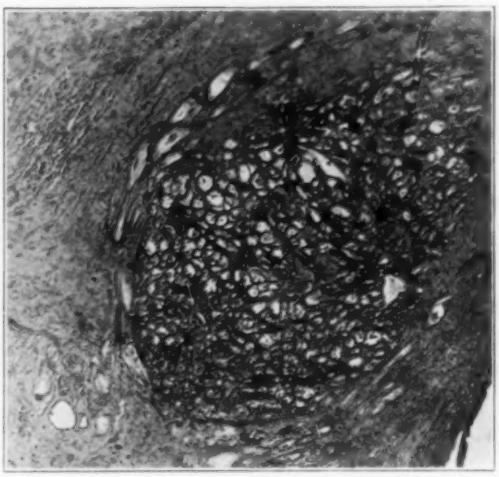

Fig. 18.—Transverse section of the base of the posterior papillary muscle of the left ventricle at its point of union with the trabecula containing the left posterior branch of the bundle (Piece 11). The extreme degree of fibrosis in and around the bundle is clearly shown.

but neither shows the marked enlargement and hypertrophy apparent in the ventricles. The right wall of the right atrium at the lower end of the crista terminalis measures 5 mm. in thickness; that of the left atrium immediately above the orifices of the pulmonary valves is also 5 mm. thick. The actual muscular wall of the right ventricle (not including any of the prominent trabeculae carneae) between the papillary muscles is 6.5 mm. in thickness, and the diameter of the wall of the left ventricle in a corresponding situation measures 16 mm. Near the atrioventricular junction the cross section of the right ventricular wall is 7 mm. and that of the left ventricle 20 mm. There is no apparent endocarditis. The cusps of all four valves are free and normal. The right atrioventricular orifice admits four fingers; into the left the entire

five can be passed as far as the proximal interphalangeal joint. The orifices of both coronary arteries are surrounded by atheromatous patches, and there is a diffuse sclerosis of both vessels throughout, possibly more marked in the left than in the right branch. Neither coronary is occluded. There is a marked patchy sclerosis of the beginning of the aorta. There is marked enlargement of the ventricular trabeculae and papillary muscles.

On opening the right side a well marked pars membranacea septi is to be observed, in the lower margin of which the bundle can be fairly well seen. Immediately in front of the fibrous septum there is marked cicatrization along the course of the bundle which can be identified under the endocardium right into the moderator band and so to the anterior papillary muscle. In the right atrium, strands of Purkinje fibers are visible on the septal wall, passing from the upper part of the crista toward the atrioventricular junction. Similar bands terminating in the same location can be seen running from the region of the coronary orifice. Blocks of tissue about 10 mm. square and 5 mm. thick were cut from the several areas recorded later. In removing such blocks of tissue it is sometimes difficult to be sure that the Purkinje fibers have been included, especially if they lie deeply in the myocardium. If the cut edge of the block be examined promptly, however, the retraction of the Purkinje bundles, always greater than that of the myocardial fibers in the perfectly fresh organ, brings about a localized dimpling of the cut surface which immediately sets all doubts at rest. In this heart we were particularly fortunate in observing the dimpling in every piece removed except numbers 4 and 5, where much cicatrization occurred.

On opening the left ventricle the bundles show less definitely. The anterior and middle limbs immediately disappear among the unusually marked trabeculae and no attempt was made to secure these. The posterior branch is plainly visible in its course toward the posterior papillary muscle and portions of it were obtained as stated later. No histologic examination was made of the left atrium.

The branches of the coronary vessels in the atrioventricular junction and those passing along the main branches of the Purkinje system are not obvious to the naked eye.

After the tissue blocks had been removed the heart was photographed and then preserved by Kaiserling's method.

The following is the list of the sites from which the tissue blocks were removed.

Right Ventricle and Atrium:

Piece 1: Moderator band (trabecula supraventricularis) near base of papillary muscle.

Piece 2: Anterior papillary muscle at site of entrance of moderator band.

Piece 3: Right branch of bundle on septal wall proximal to moderator band.

Piece 4: Stem of bundle under the endocardium of the right ventricle beneath septal cusp of tricuspid valve. This portion includes the commencement of the right and left main branches. It is greatly cicatrized. (Fig. 15.)

Piece 5: Pars membranacea septi immediately above and behind Piece 4, but, unlike the latter, which is from the interventricular part of the septum, this is from the septum between the right atrium and the left ventricle. (Fig. 14.)

Piece 6: Tissue of the coronary groove of the right atrium immediately above and including the margin of the orifice of the coronary sinus. (Fig. 16.)

Piece 7: Part of the septal wall of the right atrium immediately above and adjacent to the noncoronary cusp of the aortic valve. (We follow Keith's nomenclature in reference to the aortic cusps.)

Piece 13: Piece of ventral wall of the right ventricle for myocardial fibers.

Piece 14: Interatrial septum between coronary orifice and fossa ovalis, including the margin of the latter. This block is from the wall above and behind Piece 6.

Piece 15: Block from right atrial wall adjoining the orifice of the superior vena cava and includng the upper extremity of the crista terminalis and the muscular ring at the junction between the atrial canal and atrial appendix. From this block Pieces 16 and 17 were divided off.

Left Ventricle:

Piece 8: Left branch of the atrioventricular bundle immediately below the right coronary cusp of the aortic valve before the bundle has broken up into its three left constituent limbs. This block contains the bundle where it first appears under the endocardium of the left ventricle. (Fig. 17.)

Piece 9: Left posterior branch of the bundle in the septal wall. This was the only branch visible to the naked eye in the left ventricle. (Figs. 12 and 13.)

Piece 10: Continuation of left posterior branch passing among the trabecular tissue between septal wall and the posterior papillary muscle.

Piece 11: Base of the posterior papillary muscle at its point of union with the trabecula containing the left posterior branch of the bundle. (Fig. 18.)

Piece 12: Block from the ventricular wall at the base of the anterior papillary muscle for myocardial fibers.

Figures 10 and 11 illustrate graphically the great increase in thickness of the left ventricular wall as compared with the right, and also show the exact positions from which the various tissue blocks were removed.

TABLE 2.—Extent of Pathologic Alteration Present in the Heart

Piece No.	Fibrosis in the Atrioventricular Bundle	Piece No.	Fibrosis in the Atrioventricular Bundle
1	Diffuse	9	Well marked
2	Diffuse	10	Well marked
3	None	11	Well marked
5	Slight	14	Slight
6	Slight	15	Slight
7	None	16	None
8	Diffuse		

We shall not discuss the methods of procedure followed in the detailed study of this heart, but shall summarize briefly Professor Van der Stricht's observations on the pathologic alterations present in so far as they are of interest in connection with the clinical report and the electrocardiographic analysis. For a detailed study the reader should consult Professor Van der Stricht's monograph, to appear elsewhere.

Table 2 shows the extent of pathologic alteration present in the various pieces as enumerated in the foregoing.

It will thus be seen that with the exception of Pieces 3, 7 and 16 there is evidence of more or less marked inflammatory invasion of the bundle tract throughout, being particularly conspicuous in Pieces 9, 10 and 11 from the left posterior branch below its division, and "diffuse" in this branch just before dividing into its three constituent left limb. This inflammatory reaction is characterized by a round cell infiltration and a sclerosis of the interstitial connective tissue associated with a "cleavage" process affecting the individual Purkinje cells, "many of which undergo an exaggerated cleavage more or less pathologic

and others again divide and subdivide until they are reduced to the condition of atrophic cells in process of complete disappearance." (Figs. 12 and 13.)

In addition to this localized inflammation affecting the left posterior branch of the bundle, the majority of the segments, as already noted, show a diffuse inflammatory reaction of the bundle tract and its superficial endocardium, involving particularly in the left ventricle the terminal arborizations of the Purkinje network.

It is interesting to note further that there was a conspicuous sclerosis and atrophy of the tunica media, both of the larger arteries and of the smaller arterial branches in the atrioventricular bundle in the majority of the segments described, lesions which must have affected seriously the nutrition of the cells concerned. The coronary arteries were simply sclerosed throughout but not occluded.

It is then evident that in addition to sclerotic lesions involving in localized exaggerated foci the main stem of the atrioventricular bundle at the point of the right and left main branches (Fig. 15, Piece 4), and the left posterior branch of the bundle (Figs. 12 and 13, Piece 9), there existed throughout the entire bundle tract a most extraordinary diffuse sclerotic process profoundly affecting the entire conduction system.

SUMMARY

It is apparent that in the extent of the diffuse sclerosis present involving the terminal arborizations of the Purkinje system, this case corresponds closely to the series reported by Oppenheimer and Rothschild,[7] but that in the degree to which localized areas of fibrosis and cicatrization were present in the main stem and the left posterior branch of the bundle differs from the cases described by these observers (Figs. 12, 13 and 14), conforming in the first instance, both histologically and in the electrocardiographic records, to the type designated by them under the general term "intraventricular block" as "arborization block," and in the second instance, histologically only, to the type designated as bundle branch block.

We have hitherto accepted the large diphasic curves of greatly increased amplitude as conclusive evidence of a definite bundle branch lesion of such magnitude as seriously to interrupt the normal course of the excitation wave. In the presence of the extraordinary amount of fibrosis and cicatrization seen in the main stem and the left posterior branch of the bundle in this heart, it is difficult to believe that there was not serious interference with the normal conduction of the excitation wave in this part of the bundle tract, and yet at no time were large diphasic curves recorded. In spite of these demonstrable focal lesions, curves of relatively low voltage were invariably present.

Referring to Table 1, it will be seen that expressed in terms of amplitude, the majority of the cases cited gave curves of low voltage, so characteristic of the complex recorded in this case, and considered as indicative of a diffuse sclerosis throughout the terminal fibers of the Purkinje system. That, however, in the presence of low voltage curves of the type designated we are justified in assuming more than a predominance of such a distribution of the sclerosis and can always exclude definite localized lesions of the main stem and its branches would seem, in the light of the evidence of this heart, to be untenable.

It is further apparent that many cases showing distinct electrocardiographic evidence of bundle lesions and fibrosis of the terminal arborizations may not show any increase in the P-R interval, and in some instances, depending no doubt on the extent of the fibrosis, no, or but slight, increase in the duration of the QRS complex.

Electrocardiographic curves of low amplitude, with slight or greatly prolonged QRS interval, associated with notched initial ventricular deflections, in opposite directions in Leads I and III, and with the T-wave in a direction opposite to these initial peaks, represent essentially the ventricular complex seen in the presence of a predominant diffuse sclerosis involving chiefly the terminal arborizations, but are also compatible with associated localized focal lesions of the main stem and branches of the atrioventricular bundle.

CONCLUSIONS

1. The presence of a predominant diffuse sclerosis of the terminal arborizations of the Purkinje system gives rise to electrocardiographic curves of low amplitude, associated with a bizarre ventricular complex of a definite type.

2. Curves of large amplitude, essentially diphasic, may justly be regarded, from the experimental evidence available, as indicative of a definite totally obstructive, temporary or permanent lesion of one of the branches of the atrioventricular bundle.

3. The presence of curves of low amplitude, so characteristic of a diffuse sclerosis, did not, however, preclude the existence of definitely localized focal lesions involving the main stem and its branches.

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THE EPIDEMIC OF MUMPS AT CAMP WHEELER, OCTOBER, 1917-MARCH, 1918 *

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It is through the kindness and courtesy of Maj. Joseph Sailer, M. R. C., Chief of Medical Service at the Base Hospital, Camp Wheeler, Georgia, that this paper is presented. Methods of procedure, arrangement of the work and inspiration for a rather monotonous task were all drawn from him by the various ward surgeons who have treated mumps. It is due to him alone — and this cannot be too clearly stated — that a stupid and insignificant disease became interesting.

Patients with mumps have occupied almost half of the hospital for three months. An epidemic of such volume raises mumps to the dignity of a disease. Of approximately 18,000 men in the Thirty-First Division, there were 5,756 cases, an incidence of 32 per cent. Every third man in the division, in other words, has had mumps. Of 13,638 total admissions to the hospital to March, 1918, almost one half were mumps — to be exact, 42.2 per cent. Sporadic cases occurred from October 17, 1917, when the first patient was admitted, to November 20, when the epidemic started with 18 admissions. The next increase was on December 3, an interval of two weeks, on which day there were 46 admissions. The third increase occurred December 14, ten days later, when there were 86 admissions. The fourth rise was on December 27, with 133 admissions, and the final increase to the apex of the epidemic was on January 15, on which day there were 140 admissions. The total admissions on this day — all diseases — was 194. There were 624 cases of mumps in the hospital at one time, December 30. Corresponding falls occurred in the admission rate.

It is regrettable that such a slight, and, in a measure, preventable, disease has occupied so much time, energy and material. Lieutenant Hathcock estimates that the cost of the epidemic to the government was at least $1,000,000.

Mumps is defined by Osler as "a specific infectious disease, characterized by swelling of the salivary glands and a special liability to orchitis in males." It might be added that it is self-limited and its complications temporary and functional.

ANATOMY

Anatomic considerations should have brief mention: The parotid gland weighs from ½ to 2 ounces. It lies below and in front of the external ear, limited above by the zygoma and below by the angle of

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the mastoid and a line drawn horizontally from this point to the mastoid process. The external carotid artery is buried in it and the facial nerve crosses it transversely. Stenson's duct is 2½ inches long and opens into the mouth opposite the second upper molar. The blood supply is from the external carotid. Nerves issue from the carotid plexus of the sympathetic, fascial, and branches of auriculotemporal and great auricular.

Submaxillary Gland.—This gland weighs about 8 drams. It is placed under the lower jaw, lying on the mylohyoid, stylohyoid and hyoglossus muscles. It is separated from the parotid by the stylomaxillary ligament. The faciala artery is imbedded in a groove on the posterior surface. Its duct (Wharton's) is 2 inches long and opens at the summit of a papilla by the side of the frenum linguae. The blood supply is received from branches of the facial and lingual arteries. Nerves reach it from the submaxillary ganglion of the sympathetic and the mylohyoid branch of the inferior dental.

Sublingual Gland.—This is the smallest, weighing about 2 drams. It is placed under the mucous membrane at the floor of the mouth and is almond shaped. Its ducts (ducts of Rivinus, 18 to 20 in number) open separately on the floor of the mouth, generally one or two being joined and called Bartholin's ducts, which in turn join Wharton's duct. The blood supply is from the sublingual and submental arteries. The gustatory nerve from the posterior division of the inferior maxillary, supplies the gland.

The *structure* of these glands is that of the compound racemose type, joined by dense areolar tissue, ducts and vessels. The secretion is alkaline, water and contains ptyalin, which acts on the starch in food, changing it to dextrose or grape-sugar.

Pathology.—Not much is known of the pathology of mumps. The salivary glands are swollen. Of the entire series, one gland was removed on mistaken diagnosis. It showed a normal gland structure. Suppuration occurred in one case. It is questionable whether there was real gland suppuration here, or cellulitis of the tissues of the neck, with necrosis. Cervical and inguinal adenitis are not infrequent. The thyroid[1] gland may become enlarged during the disease. There were six cases. None of the other features of goiter appear, however. Neurotic manifestations suggest intracranial glandular involvement. In one case, in a woman, an axillary gland was swollen, producing breast pain. The pancreas is involved in some mysterious way. It may be the seat of edema or the glands at the hilus of the liver may enlarge. Except by one or the other or both of these theoretical pos-

1. Major Sailer thinks it likely that these may have been cases of thymus rather than thyroid involvement. They have, however, not been carefully studied, unfortunately.

sibilities, it is difficult to explain the jaundice, abdominal pain and vomiting of pancreatitis. Orchitis is frequent. The testicles are swollen, both or one, and tender. They may each reach the size of a man's fist. The scrotum is always red and tense. Epididymitis often precedes the orchitis. A kidney bean shaped and sized swelling in the epididymis occurs sometimes before the testicle swells. Major Sailer emphasizes the fact that the epididymitis of mumps is not characterized by the exquisite tenderness which obtains in gonorrheal infection and that the testicle is very tender. Prostatitis is not common, but occurs and may be responsible for retention of urine.

TABLE 1.—Showing the Glands Involved

Glands Involved:	Cases
Both parotids alone	2,747
Parotid, right	554
Parotid, left	627
Both submaxillaries alone	16
Right submaxillary alone	7
Left submaxillary alone	11
Both parotids and both submaxillaries	128
Both parotids and right submaxillary	38
Both parotids and left submaxillary	50
Both parotids and both sublinguals	9
Both parotids and right sublingual	1
Both parotids and left sublingual	1
Both parotids, both submaxillaries and both sublinguals	10
Both parotids, both submaxillaries and left sublingual	1
Both parotids, left submaxillary and left sublingual	1
Left parotid, left submaxillary and left sublingual	1
Left parotid, both maxillaries and both sublinguals	1
Right parotid, left submaxillary and left sublingual	1
Both sublinguals alone	1
Left sublingual alone	1
Left sublingual and left maxillary	1
Right sublingual and right submaxillary	1
Right parotid and left submaxillary	11
Right parotid and both submaxillaries	2
Right parotid and right submaxillary	24
Left parotid and right submaxillary	10
Left parotid and left submaxillary	26
Summary:	
a. Parotid glands involved in one way or another	4,243
b. Submaxillary glands involved in one way or another	440
c. Sublingual glands involved in one way or another	30

Finally there are a few cases in which mumps expresses itself by a general swelling of the neck and chest like Hodgkin's disease, a doughy gelatinous mass. Cases of this sort have been noted by Lieutenant Hathcock and Lieutenant Groover. There is no tenderness. The tissues are soft and elastic and are easily agitated. Major Sailer has called attention to a case of possible thymus enlargement. There was some swelling presternally and also in the tissues of the neck. There was alteration in the percussion note over the manubrium on change of position of the head, tympany being present when the

head was drawn back and dulness when it was brought forward. The skin showed slight edema which Major Sailer attributed to cutting off the lymph supply by the inflamed thymus. Roentgenograms showed a shadow behind the upper part of the sternum, which Major Wheat interpreted as an enlarged thymus.

One case of frontal sinusitis has been recorded. It is difficult to associate this with mumps etiologically. The glands involved in our cases have been as shown in Table 1.

Pathologic conditions associated with mumps were as shown in Table 2.

TABLE 2.—Pathologic Conditions Associated with Mumps

Condition	At or Before Onset, Cases	Developed During Onset, Cases
Measles	12	2
"Cold"	Very common	Very common
Bronchitis	13	14
Pterygium	1	0
Influenza	2	1
Laryngitis	6	0
Pneumonia	5	4
Bronchopneumonia	1	1
Tonsillitis	2	0
Malaria	1	0
Syphilis	1	0
Complications of mumps	To be mentioned separately	

Incubation Period.—This was definite in only two cases. Nurse M. was put on duty in a mumps ward January 10 and developed mumps January 24. Miss H. developed mumps February 26, having left her last case February 3. These are periods of two and three and one half weeks, respectively. Osler says that the period is from two to three weeks. In our experience, this has been generally undeterminable.

ETIOLOGY

1. *The Virus.*—Thus far the causative factor of mumps has not been definitely determined. Herb has implicated a diplococcus, which, when injected into Stenson's duct in monkeys, produces the disease. Attempts at isolation of an organism were initiated at Major Sailer's suggestion. These attempts have failed. Smears from the region of the orifice of the duct in the cheek revealed a spirillum, smaller and more slender than the treponema pallidum, in a few cases.

This was not constant, and it was concluded that the organism was the ordinary *Spirochaeta dentium*. Wright's tubes were next introduced into the orifice and smears made of the clear fluid which exuded, with negative results. At Major Sailer's suggestion, the parotid gland was aspirated with an ordinary hypodermic syringe, under aseptic conditions, one half inch below the ear. The few droplets of clear salivary secretion obtained in this way were planted on the following mediums: broth, plain agar, blood agar, human serum agar, Loeffler's medium, centrifugalized milk with a layer of cream on top, and agar covered with sterile liquid petrolatum — the last two being partially anaerobic. The results in all cases were negative, except on one occasion in which a pellicle was produced in ordinary bouillon, which showed very small cocci in flat masses. This was not reproducible, and it was concluded that the pellicle was the ordinary one which at times occurs in broth without inoculation. Smears from aspirated contents of the glands were negative. Major Sailer was very desirous of inoculating the testes of animals with the secretion, but, unfortunately, none were to be obtained. Major Thayer, on a visit to Camp Wheeler, suggested the use of salivary mediums for culture. This too, unfortunately, was not tried, due to press of work in the laboratory. It is an excellent idea and should be exploited. Noguchi's symbiotic tissue medium was not used because it could not be obtained. At my request a few tubes of 2 per cent. glucose agar and human serum were sent down by Dr. Libman from New York. Two thirds of the agar were mixed with one third serum (after melting the agar) and the tubes innoculated with the secretion aspirated from the parotid gland, and also with the blood of a patient who had developed orchitis. The tubes were rendered anaerobic by the addition of a layer of plain agar, on cooling of the mass. These ingredients were used by Dr. Plotz in isolating the organism in his typhus work. Four days after inoculation no results had appeared.[2] It is to be concluded therefore that the virus does not grow on ordinary mediums. Inoculations intraperitoneally into mice and guinea-pigs by Lieutenant Lewis of the aspirated contents of the parotid were negative. Thanks are due and gladly given to Captain Wilson and Lieutenant Ross for their kindness and assistance in the laboratory.

2. *Contact.*—There must necessarily be some influence exerted on the development of mumps by contact; otherwise the epidemic would not occur, and yet of the physicians, nurses and corps men, only

2. On the sixth day a lenticular colony, grayish yellow in color, about the size of a millet seed appeared in the middle of the medium. There were fine ciliary radiations from it. Smears showed diplococci which will be described subsequently.

twenty-nine all told took the disease — persons who had been in intimate contact with it. Five were nurses, five physicians, and nineteen corps men, of whom four were not Base Hospital men, but belonged to ambulance companies.

3. *Age.*—The age incidence was from 16 to 25 years.

4. *Sex.*—Only five cases were in women. (Eighty nurses in hospital were the only material.)

5. *Service.*—The length of service in 95 per cent. of the cases was two months.

6. *Habitat.*—The fact that most of the men lived on farms nearly all their lives may have had some bearing on the epidemic. They had not been accustomed, like their urban cousins, to epidemics of any sort, and therefore, from lack of immunity, geographically furnished good soil for the virus.

8. *Previous Condition.*—A factor of some importance was the previous condition of the men. They had been below par physically.

7. *Season.*—The winter months, October to March, were included.

9. *Immunity.*—One attack does not confer immunity. Forty-seven patients gave a previous history of mumps, in the majority of which cases the gland on the side opposite to that of the present attack had been involved; but three patients had the same gland involved twice. One patient had mumps three times. The intervals varied from two weeks to fourteen years. Lieutenant Hathcock doubts these histories and claims that one attack protects. One hundred and forty-four cases, or 3.3 per cent., had more glands develop during course than were involved at onset. The majority were right and left parotids, respectively. The intervals varied from one to seventeen days; the average was nine days, most frequently only twenty-four hours. Relapses occurred in six cases. The interval was from two to three weeks.

SYMPTOMS

The symptoms of mumps show many varied but also some constant features.

1. *Prodromal.*—Often a diagnosis of mumps may be reached before there is any swelling from the following symptoms:

a. A feeling of stiffness in the jaws.

b. Difficulty in opening mouth.

c. Condiments, especially sour ones, cause a "drawing" sensation in the jaws.

d. Dry mouth may occur at first. No sense of taste and no secretions. There may be salivation. Thirst is at times unquenchable.

e. The orifices of Stenson's duct pout and a pinkish area appears around them. They may gape wide open. This is especially noticeable in unilateral cases. A Wright's tube is introduced with ease, whereupon a clear fluid fills it.

f. The most diagnostic prodromal sign, pathognomonic, in fact, was first noted by Lieutenant Hathcock, who has personally observed and treated over 2,000 cases, and who is, from the standpoint of knowledge gained by close clinical observation of the disease, probably the best authority on mumps in the United States. The sign is tenderness just beyond the angle of the jaw on running the finger toward the angle, under the mandible. If the parotid gland is at all involved, the patient winces with pain. This occurs before any swelling can be made out. It is proper and fitting — much as eponyms are held by some to be improper — that this sign go down in the literature as Hathcock's sign. It is almost constant, it is early, it is definite and it is exclusive; therefore it is diagnostic, like Koplik's spots in measles.

2. *The Onset*.—The symptoms of onset of mumps have been many and varied.

a. Onset with no symptoms.

b. Onset with gastric disturbances and features suggesting pancreatitis.

c. Onset with pancreatitis, orchitis and urethral discharge. This occurred in two cases before the glands swelled. Lieutenant Byrne has seen one of them.

d. Onset with features of acute laryngitis and bronchitis. This was rather common in Lieutenant Hislop's series. It was especially marked during the time when measles and mumps coexisted. Cough was a marked feature. Also pain in the sternal region.

e. Grippy onset, with fever, headache, malaise, bone pains and aches, and sore throat was very common.

f. Onset with inguinal and testicular pain and backache—although orchitis did not develop — was not infrequent.

g. The ordinary onset is with pain and swelling in the jaws, stiffness, difficulty in opening the mouth, slight malaise and mild fever. According to Lieutenant Hathcock, the pain in parotid cases is greater than in submaxillary cases, because of the proximity of the tissues to the bone in the former and to the soft elastic tissues of the neck in the latter case.

3. *The Course*.—This is variable. Special symptoms of all sorts arise. Elevation of temperature is not constant; fever occurred in over 80 per cent. of the cases, however (Figs. 1 and 2).

The temperature in all cases showed a rise and fall in severity, corresponding to the epidemic proper. The range of fever is from 99 to 106 F., most commonly 99 to 101. The duration of the fever is from one to twenty-four days; the average is four days. About twenty-four hours before onset of a complication the temperature rises from one to three degrees and lasts about five days. Subnormal

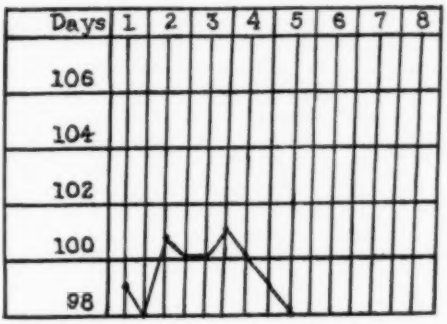

Fig. 1.—Temperature curve in an ordinary case.

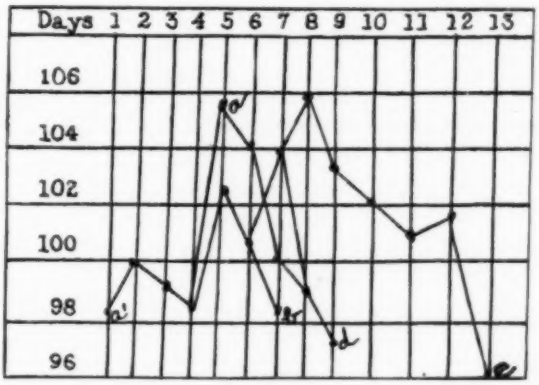

Fig. 2.—Temperature curve in orchitis accompanying mumps: a'-b, most common; a-e, all occur.

temperature may occur with cessation of the complication. The temperature may be 106 F. without obvious cause.

Vomiting, nausea, and pain and tenderness in the testicles may occur without apparent cause.

Tenderness in the epigastrium, jaundice and vomiting suggest pancreatitis.

Urinary retention may develop. Lieutenant Urey removed 32

ounces by catheter in one case. Sometimes prostatitis is associated with retention. Lieutenant Hislop is of the opinion that retention is reflex from the pain in the testicles and lumbar regions. Polyuria is not common.

Tender breasts occurred in one man and in one woman.

The patient may be doing well, apparently, and without cause develop the most marked nervous disturbances. Fainting, cold sweats, sense of collapse, diarrhea and excessive irritability may occur. Convulsions are rare, only one patient presenting a few jerky movements.

TABLE 3.—PERCENTAGES

Cases	Polymorphonuclears	Lymphocytes		Endothelials		Eosinophils	Basophils	Total Count
		Small	Large	Trans.	Others			
Normal (Stitt).....	67.5	25.0	4.0	3.0	1.5	1.5	0.4	7,125
Orchitis.....	60.2	30.2	4.3	1.7	1.8	1.8	...	10,730
Uncomplicated..... ...	51.9	36.4	2.0	3.1	3.0	3.6	...	7,060
Average (all cases)..	54.2	34.7	2.6	2.7	2.7	3.1	...	8,000

TABLE 4.—TOTAL CELLS PER CUBIC MILLIMETER

	Orchitis	Uncomplicated	Total
Number of cases.....	3	8	11
Total leukocytes.....	10,730	7,060	8,000
Polymorphonuclears.....	6,470	3,660	4,390
Lymphocytes:			
Small.....	3,240	2,570	2,800
Large.....	460	140	210
Total.....	3,700	2,710	3,010
Endothelial:			
Transitional.....	180	220	210
Others.....	190	210	200
Total.....	370	430	410
Eosinophils.....	190	200	240

All grades of deafness have been present. One patient described his ears as "wooden." Rarer symptoms, but occurring in a sufficient number of cases to warrant their notice, were epistaxis, herpes and dysphonia. A husky or small voice was most frequent.

4. *Laboratory Findings.*—The blood was examined in about 200 cases. Of 105 white counts made by Lieutenant Lewis, the average figure was 8,800, the extremes being 6,000 and 13,000. The accompanying tables and curves show the results obtained by Lieutenant Belding's blood counts in mumps (Tables 3, 4 and 5).

Lieutenant Belding concludes:

1. *Total Count.*—The uncomplicated cases showed approximately a normal total leukocyte count (7,060). In orchitis, there is a definite leukocytosis (10,730), which is largely polymorphonuclear in character, that is, 6,470 polymorphonuclear cells per cubic millimeter, nearly double the number (3,660) in the uncomplicated cases; whereas the lymphocytes show a smaller increase, that is, 3,240 vs. 2,570, or a corresponding gain of one quarter.

TABLE 5.—NUMBER AND PERCENTAGE OF CELLS

	Orchitis	Uncomplicated	Total
Number of cases	3	8	11
Total average count	10,730	7,060	8,060
Highest	14,000	12,700	14,000
Lowest	7,400	4,030	4,030
Polymorphonuclears, per cent.	60.2	51.9	54.2
Highest	82.0	61.5	82.0
Lowest	46.4	41.0	46.4
Lymphocytes:			
Small	30.2	36.4	34.7
Highest	40.6	50.0	50.0
Lowest	11.0	27.0	11.0
Large	4.3	2.0	2.6
Highest	8.0	4.0	8.0
Lowest	2.0		
Total	34.5	38.4	37.3
Highest	43.6	51.0	51.0
Lowest	13.0	27.7	13.0
Endothelials, per cent.:			
Transitionals	1.7	3.1	2.7
Highest	3.0	4.0	4.0
Lowest	1.0	2.0	1.0
Others	1.8	3.0	2.7
Highest	4.0	7.0	7.0
Lowest	...	1.0	
Total	2.5	6.0	5.4
Eosinophils, per cent.	1.8	3.6	3.1
Highest	5.5	6.0	6.0
Lowest	...	1.0	

2. *Polymorphonuclear Neutrophils.*—The polymorphonuclear leukocytes show a relatively higher percentage in the orchitic than in the uncomplicated cases. In the latter, the average (51.9 per cent.) is somewhat less than the normal (67.5 per cent.) as given by Stitt. In the orchitic cases, the percentage of polymorphonuclears is 60.2, which is less than is ordinarily found with leukocytosis of pyogenic infections.

3. *Lymphocytes.*—Conversely, the relative percentage of lymphocytes, 38.4 per cent. in uncomplicated and 34.5 per cent. in orchitic cases, is above the normal, which varies from 22 to 36 per cent. The highest orchitis case gave 43.6 per cent., the lowest 13 per cent.; while

in the simple cases the highest was 51 per cent. and the lowest 27.7 per cent. Therefore, it may be concluded that there is a slight tendency toward lymphocytosis in mumps, but in view of the small number of cases here considered (11) a definite statement cannot safely be made when the margin of increase is so small.

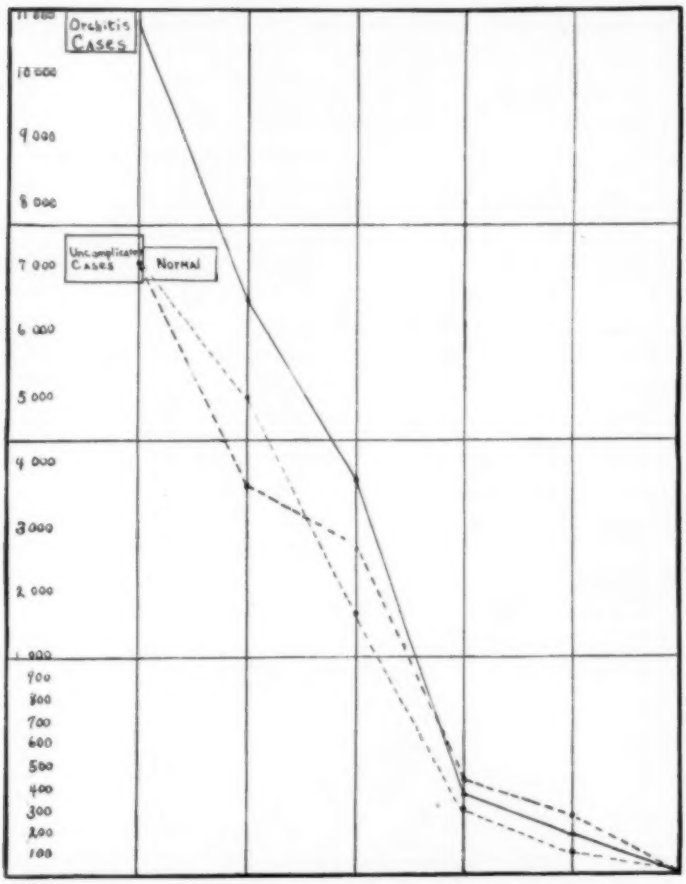

Fig. 3.—Curves showing leukocyte and differential count in mumps uncomplicated (eight cases), and in cases complicated by orchitis (three cases), from Feb. 7, 1918, to Feb. 18, 1918.

4. *Endothelials.*—This class gives a slight increase above the average, but falls within normal limits.

5. *Eosinophils.*—The increase in eosinophils is probably due to intestinal parasites (hookworm) and has nothing to do with mumps.

Red blood cells averaged 4,800,000; average hemoglobin 75 per cent. The urine in thirty cases — all kinds — was normal. Bile was present in one case of pancreatitis with jaundice, which cleared up on disappearance of the icterus. (Lieutenant Lewis.)

5. *The Physical Signs of Mumps*:

1. Hathcock's sign.
2. Pouting and pinkness of the orifices of Stenson's ducts.
3. Swelling of the face in the parotid region.
4. Doughy elasticity of the swelling.
5. Exudation of secretion from Stenson's duct on pressure of the gland externally. This was noted by Lieutenant Hathcock and others. The physical examination of the rest of the body is usually negative except in complicated cases.

COMPLICATIONS

1. *Orchitis and Epididymitis.*—Of 4,397 cases carefully considered, 611 had testicular involvement of various kinds, or 13.91 per cent.

TABLE 6.—COMPLICATIONS

Complications	Number of Cases
Orchitis, bilateral	102
Orchitis, right	231
Orchitis, left	221
Orchitis, side not mentioned	40
Epididymitis, right	4
Epididymitis, left	1
Epididymo-orchitis, right	9
Epididymo-orchitis, left	3
Total	611

Perhaps epididymitis was more common than this table indicates, because of the fact that the ward surgeons did not pay special attention to the orchitis cases beyond noting that the testicles were involved.

Thirty-seven cases developed orchitis on the side opposite to the glandular involvement of the face. Close questioning in many similar cases revealed a former infection on the other side of the face also. It is the general impression held by the ward surgeons that these thirty-seven cases may fall in this category. At any rate, the vast majority had the testicles involved on the same side as the facial swelling in unilateral cases.

Orchitis is the most frequent and most severe complication of mumps. It may occur in any period of the disease, even before the

parotid swelling, and be accompanied by urethral discharge. Orchitis begins from the third to the sixth day and lasts a variable period — from five to ten days. In not a few cases the epididymis is swollen before the testicles. Single glandular involvements were complicated by bilateral orchitis and vice versa. Orchitis makes the patients sick. There is a rise in temperature sometimes to 106 F., usually to 102. Vomiting and nausea are frequent. The patient may be covered with profuse warm perspiration. The face is anxious. Sharp shooting pains in the testicles and inguinal regions occur. There may be severe backache. With the rise in temperature, a leukocytosis is usually present from 11,000 to 14,000, as shown by Lieutenant Belding and Lieutenant Lewis. Polyuria may be present. Lieutenant Dalton has obtained histories of nocturnal pollutions in these cases which he believes are due to reflex irritations. Lieutenant Hathcock, on the other hand, thinks that continence is responsible for the condition. At any rate, close observation of this symptom has not shown it to be a constant feature. After a miserable period of from twenty-four to forty-eight hours, the testicles enlarge and are exquisitely tender. The course of orchitis is variable. After three to ten days, the testicles involute, the fever subsides, the pain and malaise depart, urination is free, the appetite returns and the patient is to be found more frequently at the canteen than in the ward.

2. *Otitis Media.*—Suppurative otitis media occurred in 20 cases of 4,397, or 0.45 per cent.

TABLE 6.—Ear Involvement

Ear Involved	Number
Otitis, bilateral	4
Otitis, right	11
Otitis, left	5

Suppuration may be profuse or mild. Pain is of varying degree of intensity. There is a rise in temperature of several degrees and at times dysphonia — nasal voice occurs. Fainting and vertigo may come on. Mastoiditis occurred in three cases which were not recorded among the total number, and were operated on by Captain Swan.

3. *Pancreatitis.*—Whether an entity or a syndrome, the symptom group is real. The patient becomes extremely ill. There is intense nausea and anorexia. Pain and tenderness in the epigastrium rapidly supervene. The temperature rises slightly. Diarrhea may occur or the patient may become jaundiced, four cases of this kind having been noted. The spleen was palpable in one case, but the patient gave a malarial history. The attack is like acute catarrhal jaundice, except

that it lasts only from three to five days. Pancreatitis occurs from the fifth to the eighth day, as a rule, but this varies. There were fourteen cases, or 0.31 per cent.

4. *Pneumonia.*—Five cases of lobar and one case of bronchopneumonia occurred during mumps. Major Sailer feared an increased pneumonia admission rate as a result of mumps, just as happened after measles, but fortunately this did not occur. Mumps has apparently little effect on the respiratory system from the standpoint of lowering the resistance to pneumonia.

5. *Bronchitis.*—There were nine cases of the ordinary type and course.

SEQUELAE

It is premature to note any sequelae in our epidemic. Sexual vigor is retained according to Osler, even with both testicles atrophied. It is not definite whether permanent deafness results from the otitis media.

DIAGNOSIS

The diagnosis of mumps is the simplest to make, and in mild cases very easy to overlook. The following are diagnostic:

1. Hathcock's sign.
2. Pink and pouting orifices of Stenson's ducts.
3. Swelling and tenderness of the salivary glands.
4. Exudation of secretion from duct on pressure of gland.
5. Pain or peculiar "drawing" sensation on eating sour food.

Differential Diagnosis:

Mumps

1. Parotids enlarged.
2. Hathcock's sign positive.
3. May be dry mouth.
4. Gums not swollen.
5. Perverted taste and pain if sour food is eaten.

Ordinary Toothache with Edema

1. Parotid not enlarged.
2. Negative.
3. May be salivation.
4. Gums swollen.
5. Neither.

Mumps

1. Fever.
2. Gums O. K.
3. Parotids swollen.
4. Epidemic.

Epulis

1. None.
2. Tumor.
3. Not swollen.
4. Not epidemic.

Submaxillary Mumps

1. Epidemic.
2. Tonsils normal.
3. Swelling is under center of mandible.

Tonsillitis with Cervical Glands

1. Not epidemic.
2. Inflamed.
3. Further back.

Course of Disease.—In uncomplicated cases, in a week the infection has subsided. The average duration — all cases — has been fourteen days; limits, two to thirty-one days. A complication prolongs the course about a week. A normal patient may suddenly develop orchitis or otitis. If pancreatitis occurs, the course is prolonged about four days. Pneumonia and bronchitis lengthen the disease by their own course.

PROGNOSIS

Of the entire epidemic, the only death was due to pneumonia. Complications are temporary. A patient without facial swelling who presents Hathcock's sign and pouting orifices of Stenson's duct will develop mumps. If, on the third day, the patient has a rise in temperature, pain in testicles, abdomen and back, with vomiting and perspiration, he may develop orchitis or pancreatitis or both. Deafness does not mean otitis. Mastoiditis has the same prognosis as in any other condition.

TREATMENT

A. Prophylaxis.—1. Careful isolation of cases for a period covering their infectivity — three weeks.

2. Of orchitis: Orchitis occurred no more frequently in the series studies by Lieutenant Byrne and Lieutenant Sherrill, whose patients got up for meals and walked about generally, than it did in Lieutenant Groover's series, whose patients stayed in bed throughout the course. Lieutenant Lewis has found that careful sterilization of the hands and protection of the glans penis did not reduce the incidence of the complication. At Major Sailer's suggestion, alternate patients were put on hexamethylenamin as admitted, 5 grains four times daily. Lieutenant Hathcock's figures show no improvement after the drug, and he concludes that "hexamethylenamin produces no perceptible results as to prevention of orchitis." Considering all figures, however, there is some benefit. Before the exhibition of hexamethylenamin, 304 cases occurred and 307 afterward, but there were only 52 cases of orchitis in which the hexamethylenamin was given before the patient had orchitis — a reduction in number by 33 per cent.

3. Of otitis: Of all measures, 2 per cent. phenolized glycerin instituted routinely — drops 2 being dropped into each nostril twice daily — at Major Sailer's suggestion, has proved the most beneficial. Before phenol in glycerin treatment began, there were seventeen cases; afterwards but three.

B. Treatment Proper.—The treatment proper of mumps is palliative, symptomatic and expectant. Our treatment has been:

1. Two compound cathartic pills on night of admission and saline in morning to insure free catharsis.

2. Dobell's gargle for mouth.

3. Hot application and camphorated oil to swelling.

4. For the pain and nervousness, acetyl salicylic acid and bromids.

5. For fever, acetyl salicylic acid and acetanilid.

6. Phenol, 2 per cent. in glycerin, 2 drops in each nostril, should be administered twice daily.

7. Hexamethylenamin has some value in reducing the incidence of orchitis; 5 grains four times daily.

8. For orchitis, support and counterirritation; any mild counter-irritant will do: *a*. ice bag; *b*. 10 per cent. icthyol ointment; *c*. guaiacol carbonate was used in a few cases with fair results; and finally,

9. Rest in bed, which is the best treatment.

A STUDY OF EIGHT CASES OF ACUTE NEPHRITIS*

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INTRODUCTION

A strictly pathologic interpretation of the term acute nephritis must mean acute inflammation of the kidneys, an inflammation primary or superimposed on a chronic process. There are, however, certain acute clinical pictures in which edema, albuminuria and other so-called renal findings may occur independent of real inflammatory disease. Hence a more consistent name for this group would be acute renal syndrome, and the cases presented here are so considered, although in certain of them actual inflammation was probably present. Moreover, in some of the cases one feels that possibly the renal manifestations are entirely secondary to a systemic disease, as is the chlorid retention of pneumonia. Two cases (7 and 8) are definitely chronic (from their histories), but they differ so strikingly from each other and are so similar in many ways to the truly acute cases that they are included for purposes of comparison. The "acuteness" of the other cases (1 to 6) is based on the absence of previous renal symptoms; for five of the six were intelligent people whose histories were quite reliable, and the sixth was partially confirmed by a daughter who is a trained nurse. That these are cases of renal edema, the absence of other causes for edema makes clear.

METHODS

The urinary chlorids were estimated by the Volhard method, plasma chlorids by the McLean and Van Slyke[1] method, blood urea and urine urea by Van Slyke and Cullen's[2] modification of Marshall's method. Practically all determinations were made in duplicate. The renal test day consisted in confining the fluids to the meals and collecting the urine in the periods described by Mosenthal.[3] The metabolism department of the Presbyterian Hospital weighed the patients and was in charge of the urine collection. All foods were weighed and fluids measured. The phenolsulphonephthalein was allowed five minutes for appearance time and the two-hour excretion determined.

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1. McLean and Van Slyke: Jour. Biol. Chem., 1915, **21,** 361.
2. Van Slyke and Cullen: Jour. Biol. Chem., 1914, **19,** 211.
3. Mosenthal: THE ARCHIVES INT. MED., 1916, **16,** 733.

The urea and chlorid indexes were determined over two-hour periods and calculated according to McLean's[4] formulae, with this exception, a constant weight was used for the entire period of observation, a weight as near the patient's normal as could be estimated. It seems obvious that a change in the index due to the loss of 40 pounds of edema would not express a true change in renal function.

REPORT OF CASES

CASE 1.—No. 342213. Woman, aged 27; admitted March 6, 1917. Complaint, headache for five days.

Family History.—Mother died of tuberculosis.

Personal History.—Malaria at 22 years; tonsillitis at 25 and 26 years; has a rash when she eats strawberries; dyspnea on exertion for four months; no nocturia or any renal symptoms.

Present Illness.—Edema of ankles for two or three weeks; frontal headache twelve days before admission, returning again five days before admission and continuing up to admission; no other symptoms; no urinary abnormalities.

Physical Examination.—Slight general edema; some pyorrhea; large red tonsils; heart moderately enlarged to the left; blood pressure, 188/150; suggestion of fluid at left base; right kidney palpable; sinuses negative; eyegrounds normal; Wassermann negative. Blood: hemoglobin,. 91 per cent.; red blood corpuscles, 4,980,000; white blood corpuscles, 10,000. Urine: specific gravity, 1.011; albumin, faint trace; hyaline and granular casts; no red blood corpuscles. Nephritic test day: day specimen, 1,455 c.c.; specific gravity, 1.008-10; night specimen, 765 c.c.; specific gravity, 1.013.

Course.—Under treatment the edema disappeared in two weeks and in three weeks the blood pressure was 130/90; during her five weeks in the hospital the specific gravity of the urine varied from 1.008 to 1.020 and at no time were there red blood corpuscles in it.

Readmitted June 20, 1917, for functional study. Aside from tiring very easily, the patient feels quite well; no edema; blood pressure, 122/70. Blood: red blood corpuscles, 5,500,000; hemoglobin, 112 per cent.; white blood corpuscles, 9,400. Urine: specific gravity, 1.012-1.015; albumin, trace; 1 hyaline cast. Renal function entirely normal throughout.

Phenolsulphonephthalein, 60 per cent.; Ambard, 111; blood urea, 0.20 gm. per liter; actual plasma chlorid, 6.03 gm. per liter; calculated plasma chlorid, 5.97 gm. per liter; threshold, 5.67 gm. per liter.

O. P. D., July 29, 1917. Blood pressure, 130/80; no edema.

Feb. 24, 1918, patient reported to be sick in bed out of town; nature of illness unknown.

CASE 2.—No. 34165. Man, aged 27 years; admitted Feb. 27, 1917. Complaint, swelling of legs and ankles for two days.

Family History.—Father had rheumatism; mother died at 52 years of kidney trouble.

Personal History.—Rheumatic fever when a child; hives at 15 years; no renal or cardiac symptoms before present illness.

Present Illness.—Nocturia for two or three weeks; slight cough for one week; three days prior to admission, frontal headache lasting one day; next day, while bathing, noticed that his feet were swollen; no nausea, urinary changes or dyspnea; some palpitation.

Physical Examination.—Marked general edema; severe pyorrhea; heart slightly enlarged to the left; blood pressure, 154/90; ophthalmoscopic examina-

4. McLean: Jour. Exper. Med., 1915, **22**, 212.

tion negative except for slightly hazy disks; blood culture and Wassermann, negative. Blood: hemoglobin, 70 per cent.; red blood corpuscles, 3,570,000; white blood corpuscles, 7,600. Urine: specific gravity, 1.033; albumin, very faint trace; few red blood corpuscles; occasional hyaline and granular cast. Nephritic test: day specimen, 598 c.c.; specific gravity, 1.011-1.028; night specimen, 1,315 c.c.; specific gravity, 1.015.

Course.—After nine days with restriction of salt, water and nitrogen the edema disappeared; the blood pressure dropped to 118/80 and the urine became perfectly normal except for an occasional hyaline cast.

March 20.—Hemoglobin, 70 per cent; red blood corpuscles, 4,020,000.

May 31, 1917.—Urine: albumin, negative; microscopic examination, negative; Ambard, 470; blood urea, 0.15 gm. per liter. Actual plasma NaCl, 6.25 gm. per liter; calculated plasma NaCl, 6.09 gm. per liter; threshold, 5.78 gm. per liter.

Feb. 4, 1918.—Patient in France with the American Expeditionary Forces; said to be in good health.

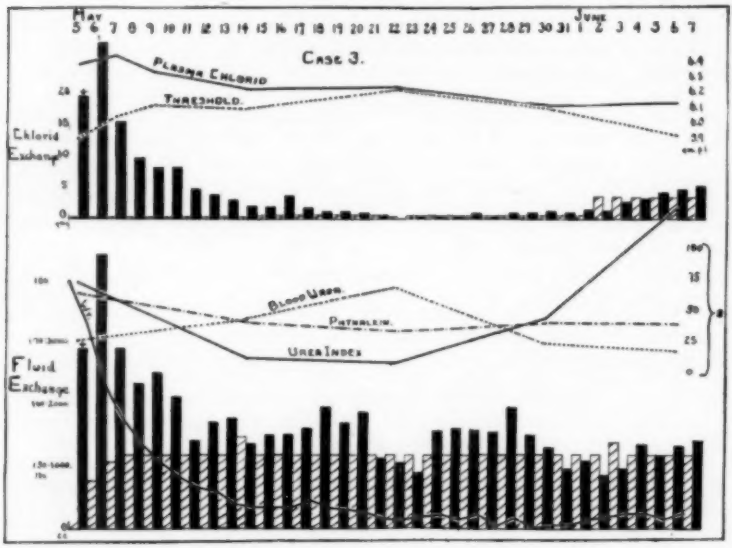

Chart representing chlorid and fluid exchange in Case 3. *= mg. per 100 c.c. for blood urea; per cent. for phenolsulphonephthalein; indirect for urea index (McLean).

Case 3.—No. 34795. Man, aged 35; admitted May 4, 1917. Complaint, headache and swelling of body for two weeks. Family history negative.

Personal History.—Works as a brakeman and is subjected to considerable exposure; has "grippe" every winter; has had frequent frontal morning headaches since childhood; tonsillitis and quinsy six years prior to admission and tonsillitis again four years prior to admission; tonsillectomy one year prior to admission; no sore throat since; nocturia for four months; no dyspnea or edema.

Present Illness.—Onset three weeks prior to admission with coryza, severe headache, pains in chest—"grippe;" he worked on for a week and then went to bed for three days; on returning to work his body began to swell, he became

dyspneic and his urine became scanty and "dark brown" in color; for the previous ten days he had been on a diet of milk, cereals and broth and for the previous five days his urine had been clearer and of larger quantity; no nausea or vomiting; edema had been decreasing in the previous four days.

Physical Examination.—Diffuse edema, mainly below fourth rib; slight signs of fluid at both bases; mild coryza; heart, lungs and abdomen normal; blood pressure, 145/95; Wassermann, negative. Blood: hemoglobin, 70 per cent.; red blood corpuscles, 4,240,000; white blood corpuscles, 11,300. Urine: specific gravity, 1.017; albumin, faint trace; occasional hyaline casts; no red blood corpuscles. Nephritic test day: day specimen, 852 c.c.; specific gravity, 1.010-30; night specimen, 505 c.c.; specific gravity, 1.019.

Course.—Under treatment the edema disappeared and the blood pressure reached normal (122/80) in six days; July 3 the blood was, red blood corpuscles, 5,400,000; hemoglobin, 75 per cent.

Oct. 31, 1917.—The patient feels perfectly well and is at work; no dyspnea, edema or nocturia; blood pressure, 120/60.

January, 1918.—Feeling fine, working as a brakeman again; blood pressure, 108/60; no symptoms at all. Red blood corpuscles, 4,576,000; white blood corpuscles, 11,800; hemoglobin, 97 per cent. Urine: albumin, very faint trace; microscopic examination, negative. Ambard, 65; blood urea, 0.2 gm. per liter; actual plasma NaCl, 6.6 gm. per liter; calculated plasma NaCl, 5.89 gm. per liter; threshold, 6.33 gm. per liter.

CASE 4.—No. 34213. Woman, aged 26, married; admitted Feb. 20, 1917. Complaint, swelling of face and feet; blood in urine for two weeks. Family history negative.

Past History.—Frequent attacks of "grippe" the last five weeks prior to admission; four or five months prior to admission, fleeting attacks of dizziness; four months prior to admission, at night had an epileptic attack in which she bit her tongue and was unconscious for ten minutes. A similar attack occurred five weeks and again six weeks later; no urinary or cardiac symptoms before present illness.

Present Illness.—Five weeks prior to admission the patient had an attack of "grippe" with sore throat, malaise, general pains, chills and fever, headache and sweats; was in bed five days; after being up about two days she noticed confluent red and blue streaks over her feet and legs to her knees and her feet were so sore that she could not walk; there was no scaling of the eruption; several days later she began to vomit everything; this lasted about two weeks but she did not go to bed; toward the end of this time she began to have swelling of the feet and face and dyspnea on exertion, and at about the same time she began to have blood in the urine. These symptoms have continued to the present; occasional frontal headaches for the previous ten days; nocturia for the previous two or three weeks; her edema had begun to decrease a few days before admission.

Physical Examination.—Pale; slight edema of legs; fading purple spots on both legs and on outer side of left leg an area 6 cm. in diameter indurated, inflamed and tender in center; bad teeth; large cryptic tonsils; heart slightly enlarged to left, with soft, blowing, systolic murmur at apex; blood pressure, 132/86; eyegrounds, normal; Wassermann, negative; roentgenogram of kidneys, negative; urine culture, negative. Blood: hemoglobin, 85 per cent.; red blood corpuscles, 3,850,000; white blood corpuscles, 12,000. Urine: grossly bloody; specific gravity, 1.016; albumin, trace; hyaline, granular and blood casts. Nephritic test day: day specimen, 642 c.c.; specific gravity, 1.008-12; night specimen, 612 c.c.; specific gravity, 1.010.

Course.—The edema quickly disappeared but the hematuria persisted grossly for about three weeks and there was microscopic blood in the urine on discharge three months after admission; while in the hospital she had two typical epileptic seizures; blood pressure was between 105/76 and 130/78.

Readmission, Nov. 12, 1917. Feels fine and has gained greatly in strength; no edema, headaches or epileptic attacks; no urinary symptoms.

Physical Examination.—No edema; good color; heart unchanged; blood pressure, 105/75; red blood corpuscles, 4,700,000; hemoglobin, 85 per cent.; white blood corpuscles, 11,400. Urine: specific gravity, 1.028; albumin, very faint trace; no casts or red blood corpuscles; salt concentration, 0.76 per cent.; phenolsulphonephthalein, 67 per cent.; Ambard, 72; blood urea, 0.26 gm. per liter.

CASE 5.—No. 34891. Man, aged 46; admitted May 14, 1917. Complaint, swelling of body for one week. Family history negative.

Personal History—The patient's low mentality and poor command of English made the history somewhat unsatisfactory; apparently quite healthy up to present illness; nocturia two or three times for all his life but no other symptom of renal disease; no scarlet fever; one brandy a day regularly.

Present Illness.—Onset one week before admission, with a severe headache that lasted for two days; on the third day he noticed the diffuse edema; on admission he complained of sore throat and slight cough of one day's duration; no history of dyspnea or urinary changes.

Physical Examination.—General edema and anasarca; very marked oral sepsis with gingivitis and ulceration; large heart with soft systolic blow at apex; blood pressure, 175/80; liver palpable; ophthalmoscopic, negative; Wassermann, negative. Blood: hemoglobin, 85 per cent.; red blood corpuscles, 5,180,000; white blood corpuscles, 11,800. Urine: specific gravity, 1.023; albumin, 1.5 per cent.; many hyaline and granular casts; few red blood corpuscles.

Course.—On restriction of salt, nitrogen and water the edema disappeared, blood urea returned to normal from its high figure, 1.41 gm. per liter, the blood pressure dropped to 130/66, and on discharge the urine showed no blood or casts. During recovery red blood corpuscles went to 4,140,000 and hemoglobin to 65 per cent.

June 22, 1917.—Blood pressure, 160/90.

Dec. 29, 1917.—Patient's family reports that he is perfectly well; he refuses to return for observation.

CASE 6.—No. 34128. Man, aged 26, admitted Feb. 24, 1917. Complaint, swelling of face for ten days. Family history: Mother died of tuberculosis.

Personal History.—Works as a compositor (eight years) but has always been very careful with the lead; Bell's palsy eight years prior to admission, with two exacerbations since; no sore throats; no cardiorenal symptoms before present illness.

Present Illness.—Onset ten days previous to admission, with swelling of face; two or three days previously he had a cough; for one day he had noticed swelling of the ankles; absolutely no other symptoms could be elicited.

Physical Examination.—General edema; residual right facial paralysis; carious teeth; large tonsils; few palpable glands in neck and axilla; heart enlarged to left; blood pressure, 178/112; ophthalmoscopic examination, negative; Wassermann, negative; roentgenogram of teeth and sinuses, negative; marked typus femininus, with soft skin, scanty body hair and transverse pubescence. Blood: hemoglobin, 79 per cent.; red blood corpuscles, 4,350,000; white blood corpuscles, 7,600; no stippling. Urine: specific gravity, 1.017; albumin, heavy trace; hyaline and granular casts; few red blood corpuscles; lead negative.

Course.—Progressively downward; edema increased and hydrothorax and ascites developed; March 24, blood $CO_2 = 24.8$ mm. Hg (acidosis was corrected easily with bicarbonate). April 11 his gums began to bleed and a week later he was twitching and irrational and diarrhea had set in; these symptoms continued until death. April 21 the kidneys were decapsulated and the patient died twelve hours later. Postmortem examination was not obtained.

The blood pressure remained practically constant; the urinary picture did not change except that the specific gravity went as high as 1.022 at one time; the blood became anemic in type; red blood corpuscles, 3,300,000; hemoglobin, 65 per cent.; the blood urea increased steadily. About one week before death a number of small ulcers about two to three mm. in diameter appeared on both legs and thighs; they resembled small vesicles or pustules with the top scraped off.

The kidney at operation was about normal in size, with a smooth surface and an easily stripping capsule. The kidney tissue did not bulge when the capsule was cut. A small piece of kidney tissue was removed for microscopic examination. "The tissue was not very well fixed, but the lesion was very definite and striking. Every glomerulus was affected. Each showed more or less proliferation of the capsular epithelium. In some there was the characteristic crescent formation. Adhesions between the glomerulus and the capsule were common, and some of the glomeruli were partially organized. There was, in places, a considerable increase in connective tissue, especially in the neighborhood of the glomeruli. There was very little in the way of a cellular reaction and the few scattered cells seen in the interstitial tissue were chiefly of the mononuclear variety. A few polynuclears were noticed in some of the tubules. Tubular changes were not very marked; a good many were filled with a cellular debris with, in places, a little mixture of blood, and some were dilated. The vessels were practically unaffected.

"The lesion was essentially a glomerulonephritis. I should say that the process had been going on for some time, but in the absence of marked scarring, I should designate the lesions a subacute glomerulonephritis." This description of the section was kindly made by Dr. R. A. Lambert.

CASE 7.—No. 33341.—Woman, aged 25, single; admitted Dec. 31, 1916. Complaint, kidney trouble for four weeks. Family history negative.

Past History.—Diphtheria at 19, with antitoxin; no reaction; frequent colds and sore throats; no edema or nocturia. Previous admission to this hospital April 25, 1914 (No. 13347), with the diagnosis "gastric ulcer and hematemesis"; she improved on a Lenhartz diet and was discharged May 18, 1914; at this time she showed no edema; blood pressure, 100/78; heart 11.5 cm. to the left in fifth interspace; urine: specific gravity, 1.016-37; albumin, faint trace; occasional hyaline cast. Patient still complained of some pain immediately after eating.

Present Illness.—Edema of ankles for about four weeks; puffiness of face and swelling of abdomen for two weeks; weakness and mild morning headaches for about the same length of time; dull aching pain in lumbar region worse on right and on lying down, for about two weeks; no nausea, nocturia, dyspnea or eye symptoms; no definite history of hematuria; chill and fever the day before admission.

Physical Examination.—Pale; slight edema of face, marked edema of legs; bad pyorrhea; tonsils deep and cryptic; heart 5 cm. to right in fourth interspace, 14 cm. to left in fifth; blood pressure, 154/102; few fine râles at both bases; eyegrounds normal; Wassermann negative. Blood: hemoglobin, 82 per cent.; red blood corpuscles, 4,800,000; white blood corpuscles, 12,000; polymorphonuclears, 56 per cent. Urine: specific gravity, 1.050; albumin; boils solid; hyaline casts; no red blood corpuscles. Nephritic test day: day specimen, 748 c.c.; specific gravity, 1.016-26; night specimen, 604 c.c.; specific gravity, 1.022.

Course.—Patient ran an up-and-down course with periods of absence of edema, although there was still some present in her ankles on discharge. February 26, tonsils were removed and at other times various decayed teeth were taken care of or extracted; January 5, had headache and vomiting lasting for two days; January 14, headache, chill, fever, pain in chest, red throat, but lungs were negative; February 19, some diarrhea; March 24, hemoglobin, 40 per cent.; red blood corpuscles, 3,400,000; blood pressure as follows: December 11, 130/88; December 31, 146/106; January 16, 138/92; January 25, 122/82; Feb-

ruary 7, 148/108; February 20, 120/90; March 15, 130/90; April 12, 116/90; May 22, 108/70. Urine: specific gravity varied from 1.012-27; always considerable albumin and numerous hyaline and granular casts; frequently red blood corpuscles, but none on discharge, May 22. January 14 and 15, fever of 103 F.; January 23 and February 17, temperature 100.6 F.

Readmission June 29. Still weak and somewhat dyspneic on exertion; ankles edematous; heart 3 by 11 cm.; blood pressure, 106/68. Blood: hemoglobin, 65 per cent.; red blood corpuscles, 4,410,000; white blood corpuscles, 9,000. Urine: specific gravity, 1.014; albumin, trace; no casts; occasional red blood corpuscles. Phenolsulphonephthalein, 50 per cent.; Ambard, 50; blood urea, 0.28 gm. per liter; actual plasma NaCl, 6.28 gm. per liter; calculated plasma NaCl, 5.86 gm. per liter; threshold, 6.04 gm. per liter.

Dispensary notes: August 3, occasional headaches; slight edema of the legs; no nocturia; blood pressure, 110/70. Urine: 1.022; faint trace of albumin; no casts. September 7, feels fine; no edema or dyspnea. Urine: 1.029; albumin, faint trace; no casts. October 19, edema of legs. Urine: 1.030; albumin, faint trace; no casts.

Readmitted, Nov. 27, 1917. No nocturia; edema of ankles every night; had been on as complete a salt-free diet as is possible outside the hospital; had been unable to go back to work; some dyspnea on exertion; had been having attacks of dyspnea without apparent cause every day for the previous two months; no asthmatic symptoms; no sense of oppression over chest. Physical examination showed good color; slight edema of ankles; heart, 2.5 cm. to right in fourth interspace and 10.5 cm. to left in fifth interspace; blood pressure, 115/85; lungs clear. Urine: specific gravity, 1.015-30; albumin, trace; microscopic examination, negative; NaCl, 0.54 per cent. to 0.17 per cent.; daily output, 3.5 to 2.6 gm. Blood: hemoglobin, 80 per cent.; red blood corpuscles, 4,304,000; white blood corpuscles, 6,600. Ambard, 87; phenolsulphonephthalein, 65 per cent.; blood urea, 0.21 gm. per liter. Actual plasma chlorid, 6.50 gm. per liter; calculated plasma chlorid, 5.90 gm. per liter; threshold, 6.21 gm. per liter.

March, 1918.—Patient feels much better. No edema; much less weakness.

Case 8.—No. 33338. Boy, aged 17; admitted Dec. 2, 1916. Complaint, swelling of body. Family history negative.

Personal History.—Never robust; at three years he began to have headaches, which at about 11 years increased in frequency for three or four years; recently they had come about every five weeks; the last one five weeks before admission; these headaches began in the morning and lasted all day; patient's mother said that at 3 years of age he had swelling of the feet that prevented his walking; his father said that one year previous he had swelling of the legs and was in bed for two weeks, after which it disappeared, not to return until the present illness.

Present Illness.—Onset November 6, with cold, sore throat, pains all over body, headache, fever and vomiting; went to bed and in about two days the feet began to swell and abdomen, face and hands; at the same time he passed small amounts of bloody urine; with the appearance of edema the headache and vomiting disappeared; for a week before admission the diet was restricted to milk, eggs, soups, bread and butter; on admission the patient said he felt fine.

Physical Examination.—Marked general edema; fluid in both chests and abdomen; tonsils moderately large, but apparently not inflamed; no hair on face or chest, transverse pubescence; skin very soft; heart 12 cm. to left in fifth interspace; eyegrounds normal; Wassermann negative; urine culture showed a nonhemolytic streptococcus; blood pressure, 142/90. Blood: hemoglobin, 95 per cent.; red blood corpuscles, 4,670,000; white blood corpuscles, 20,400. Urine: grossly bloody; specific gravity, 1.020; albumin, 1.2 per cent.; large granular and red blood corpuscle casts; many red blood corpuscles and white blood corpuscles.

Course.—Although the patient began to lose weight from the beginning, the marked diuresis did not begin for about one month and it was almost three months before the edema had completely disappeared. January 9 there was a generalized urticaria which disappeared in about four days. February 12: hemoglobin, 50 per cent.; red blood corpuscles, 3,400,000; white blood corpuscles, 10,200. March 19: tonsillectomy; recovery uneventful. Blood pressure: December 4, 162/105; December 11, 138/80; Dec. 20, 164/100; January 21, 206/140; February 7, 164/122; February 15, 128/90; March 6, 152/106; March 12, 126/94; March 20, 152/84. Urine: specific gravity varied from 1.014 to 1.026; red blood corpuscles persisted in urine until about the middle of February.

Dispensary Note: April 10, feels fine; no symptoms except nocturia; physical examination shows slight edema of ankles; blood pressure, 160/95. Urine: 1,015; albumin, 0.4 per cent.; no red blood corpuscles.

Readmission, April 30. Had had no edema, still had nocturia; felt fine. Physical examination: good color, no edema; blood pressure, 155/90; red blood corpuscles, 4,000,000; hemoglobin, 86 per cent.; white blood corpuscles, 12,000; phenolsulphonephthalein, 38 per cent.; Ambard, 22; blood urea, 0.2 gm.; actual plasma NaCl, 6.5 gm. per liter; calculated plasma NaCl, 5.9 gm. per liter; threshold, 6.2 gm per liter. Urine: specific gravity, 1.022; albumin, heavy trace; hyaline and granular casts; no red blood corpuscles; salt concentration, 0.4 per cent.

Dispensary Note: July 2, no edema; never felt better; blood pressure, 175/95. October 1: feels fine; no edema; blood pressure, 155/100. December 31: no gastric, intestinal or cardiac symptoms; no edema or headache; blood pressure, 180/100. Urine: specific gravity, 1.011; albumin, heavy trace; hyaline and granular casts.

CLINICAL SUMMARY

The two cases (7 and 8) whose histories show that their disease has been of long duration, exhibit no special clinical characteristics, and are, therefore, grouped with the rest of the series in the clinical discussion. The average age was about 26 years; only one patient was over 35 years, Case 5, who was 46. The *past histories* of three of the six "acute" cases were absolutely negative from a renal point of view; one patient, Case 1, had dyspnea on exertion; Case 3 had nocturia for four months and the patient (5), whose history was not very reliable, said that he had had nocturia all his life. Searching for an etiology, we find tonsillitis in three cases, hives and rheumatic fever in one and epilepsy in another. The *present illness* varied from one to three weeks, with the onset, edema in four cases "grippe" or some acute infection in three, nocturia in one, and headache in another. Edema was marked in all except Cases 1 and 4, in which it had apparently begun to disappear before admission. Every patient but one, the fatal case, had headaches. Some acute infection, "grippe," sore throat, or cough, was present in six of the eight cases. Hematuria occurred in two cases (4 and 8); nocturia in four cases, and oliguria in two. Lumbar pain was found in only one case. There was a history of dyspnea on exertion in three cases, all acute. The only constant feature, therefore, was edema; with headaches in every case but one. The other symptoms occurred quite accidentally, distributed indifferently between the acute and chronic cases.

On *physical examination* there was general edema in six cases and slight dependent edema in the other two (1 and 4); the blood pressure was above normal in all the cases, ranging from 136/86 mm. to 180/150 mm.; but in every instance it returned to normal while in the hospital, rising again after discharge in Cases 5 and 8 only. The heart was normal in size in Case 3, slightly enlarged in Cases 2, 4, 7 and 8, moderately enlarged in Cases 1 and 6, and considerably enlarged in Case 5. It is worthy of mention that in the latter three cases the systolic blood pressure was over 174 mm., whereas the next highest pressure was 154 mm.; in other words, an apparent relation between the degree of hypertension and cardiac hypertrophy. Pyorrhea was found in six cases, tonsillar abnormality in four cases, while Cases 3 and 8 showed no foci of infection. Leukocytosis (over 10,000) was present in six cases, occurring in the two cases that showed no infection at the onset. There was, during the hospital stay, definite anemia in every case, and all except Cases 1 and 3 showed red blood cells in it. No constant relationship between the amount of hematuria and the degree of anemia could be demonstrated. There were no other significant physical findings. Albuminuria in varying amounts was found in every case, and all except Cases 1 and 3 showed red blood cells in the urine, while two cases (4 and 8) were grossly hematuric. The four cases with only a trace of albumin on admission had the most favorable courses, but the influence of the total output of urine on the concentration of albumin, as shown by a simple qualitative test, will help to explain this observation. Every case had hyaline casts, and the grossly hematuric cases had red blood cell casts.

From the history and clinical examination one cannot separate these cases into definite categories. Edema, hypertension, albumin and casts were constant, but other details were quite promiscuously distributed; for example, the two cases with gross hematuria were otherwise quite unlike, and the case with the highest blood pressure showed among the fewest abnormalities. There is, however, a single exception in Cases 5 and 6, for they show similar histories and the clinical findings correspond rather closely; but if we compare their courses we see that one patient died while the other improved most remarkably. It seems, therefore, that a clinical classification of this series is quite impossible.

The course in each case is summarized in the case history, but there are certain points that are worth noting. During the hospital stay three of the acute cases made a complete symptomatic recovery, two improved greatly and one died; of the chronic cases, one improved very much, and the other hardly at all. The discharge physical examination showed only one case (7) with edema, and none with hypertension, but the anemia in each instance persisted. Those patients who

TABLE 1.—DATA IN CASE 1*

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sulphone-phthalein	Urea Index				Chlorid Index †				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Threshold
March 7- 8	134.0	1,500	446	2.0	1.9	38	0.1	7.8	5.7	135	5.8	4.3	5 94	5.82	5.74
8- 9	130.8	1,500	900	2.0	4.0										
9-10	137.5	1,500	1,500	2.0	6.9										
10-11	128.5	2,000	1,050	0.6	1.9										
11-12	.....	2,000	1,335	0.8	0.5										
12-13	129.5	1,500	2,000	0.8	0.6										
13-14	128,5	1,500	1,550	0.8	0.5										
14-15	128.5	1,500	300+	0.8	0.4										
15-16	129.0	1,500	1,070	0.8	0.5										
16-17	128.0	1,500	1,130	0.8	1.2	48	0.22	7.0	17.5	141	3.1	7.8	5.80	5.85	5.57
17-18	127.5	1,500	1,605	0.8	1.2										
18-19	127.0	1,500	1,670	0.8	1.3										
19-20	127.0	1,500	1,418	7.8	1.5	..	....	...	....	...	0.4	0.7	5.89	5.62+	5.89‡
											0.4	1.1	5.96	5.62+	5.96§
20-21	128 0	1,500	1,430	0.8	2.9	..	....	...	....	...	1.5	2.9	6.14	5.74	6.02¶
21-22	128.0	1,200	710	0.8	1.4										
22-23	127.5	1,500	1,000	0.8	2.1										
23-24	128.0	1,500	1,190	0.8	1.4										
24-25	127.5	1,500	1,300	0.7	1.4										
25-26	127.5	1,500	1,450	0.8	2.7										
26-27	127.0	1,500	1,180	0.7	0.9										
27-28	127.5	1,500	1,950	0.7	1.5										
28-29	128.0	1,500	1,440	0.7	0.6										
29-30	127.5	1,500	1,270	0.7	0.5										
30-31	128.0	1,500	1,510	3.2	1.4										
31-Apr. 1	127.0	1,500	1,472	3.2	2.8	65	0.18	5.1	13.6	140	2.5	6.7	5.94	5.82	5.74
1- 2	127.0	1,500	630	3.2	0.8										
2- 3	128.0	1,500	1,400	3.2	3.3										
3- 4	127.0	1,800	2,120	3.2	3.9										
4- 5	127.0	1,800	1,330	3.2	1.9										
5- 6	125.6	1,800	1,410	3.1	2.9										
6- 7	126.5	1,800	2,150	3.1	4.1										
7- 8	127.0	1,800	1,830	3.1	3.5										
8- 9	.....	1,800	2,370	3.1	3.6										
9-10	128.5	1,800	1,730	3.2	3.9										
10-11	128.0	1,800	2,280	3.2	4.8										
11-12	128.5	1,560	2,356	...	5.0	64	0.19	2.5	11.6	75	2.7	12.43	6.03	5.90	5.74
June 20	.....	.....	.....	...	...	60	0.20	2.8	18.1	111	2.3	20.5	6.01	5.97	5.67

* Fluids expressed in c.c.; urinary chlorids in gm.; blood concentration in gm. per liter.
† Weight for index = 61 kg.
‡ At 1:30 p. m.; 7 gm. NaCl at 2 p. m.
§ At 3:30 p. m.
¶ At 1:20 p. m.

TABLE 2.—DATA IN CASE 2

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Mar. 1	158.5	1,500	1,170	2.4	12.9	44	0.38	20.0	22.5	98	3.9	4.3	6.33	5.79	6.16
1- 2	154.0	1,500	2,450	2.4	16.5										
2- 3	149.0	1,500	2,480	2.4	14.9										
3- 4	144.5	1,500	1,606	2.4	9.6	56	0.31	12.1	18.4	94	7.7	19.6	5.99	6.07	5.54
4- 5	141.5	1,500	2,065	2.4	8.4										
5- 6	137.5	1,500	2,060	2.4	10.6										
6- 7	133.0	1,480	2,120	0.5	5.1										
7- 8	130.5	1,500	1,940	0.5	4.0										
8- 9	130.5	1,500	1,330	0.3	2.9										
9-10	129.5	1,500	1,410	0.6	3.2										
10-11	129.5	1,500	1,000	0.7	2.5										
11-12	128.5	1,500	920	0.7	2.0										
12-13	129.0	1,500	1,540	0.6	2.3										
13-14	127.5	1,500	1,250	0.7	0.8										
14-15	128.0	1,500	895	0.7	0.8	48	0.37	9.2	22.4	70	1.4	3.5	5.78	5.74	5.65
15-16	127.5	1,500	636	7.7	0.8	..	....	...	....	...	0.42 0.82	0.6 0.68	5.84 6.03	5.62+ 5.62+	5.84—† 6.03—‡
16-17	128.5	1,500	1,060	0.7	2.1										
17-18	128.5	1,450	1,158	3.8	3.2	..	....	...	....	...	2.3	4.3	6.60	5.73	5.84
18-19	128.0	1,450	960	3.8	4.2										
19-20	129.0	1,500	1,000	3.8	5.1										
20-21	128.0	1,450	750	3.7	4.2										
21-22	128.0	1,500	735	3.7	6.1										
22-23	131.3	1,500	1,280	3.5	3.4										
23-24	129.5	1,500	810	3.7	1.6										
24-25	130.0	1,500	1,010	3.7	3.0										
25-26	130.0	1,500	1,980	3.8	2.9										
26-27	130.0	1,500	1,040	3.8	5.8										
27-28	127.0	1,500	1,200	3.5	5.7	51	0.23	6.0	18.1	118	3.3	10.0	5.90	5.88	5.60
28-29	130.0	1,500	1,270	3.7	4.1										
29-30	130.0	1,500	880	3.6	3.9										
30-31	131.5	1,500	1,130	3.4	3.5										
31-Apr. 1	130.5	1,500	1,600	3.4	6.4										
1- 2	131.0	1,500	950	3.6	6.0										
2- 3	133.0	1,500	1,220	3.5	6.4										
3- 4	130.5	1,500	1,410	3.5	3.9										
4- 5	129.5	1,500	880	4.4	5.2										
5- 6	129.5	1,500	600	4.6	2.5										
6- 7	130.3	1,500	1,700	4.6	8.4										

* Weight for index = 62.7 kg.
† At 1:30 p. m. 7 gm. NaCl at 2 p. m.
‡ At 3:30 p. m.

TABLE 2.—DATA IN CASE 2—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
April 7- 8	131.3	1,500	945	4.5	5.5										
8- 9	133.0	1,500	955	4.6	6.2										
9-10	130.5	1,500	1,547	4.4	6.5	60	0.2	4.1	16.4	116	3.5	13.6	5.89	5.93	5.58
10-11	130.5	1,500	570	4.4	1.9										
11-12	130.5	1,500	660	4.6	2.0										
12-13	132.0	1,500	1,410	4.6	4.1										
13-14	134.0	1,500	1,750	4.6	5.0										
14-15	132.5	1,500	1,140	4.6	4.0										
15-16	133.0	1,500	1,300	4.6	2.8										
16-17	132.0	1,500	1,940	4.6	7.3										
17-18	133.0	1,500	1,380	4.6	1.6										
18-19	135.5	1,800	1,913	4.4	4.5										
19-20	132.5	1,800	1,080	4.6	4.6										
20-21	135.0	1,700	1,500	4.6	2.7										
21-22	134.5	1,800	1,300	4.6	3.7										
22-23	135.0	1,700	1,410	4.6	5.6	*									
23-24	.....	.....	856	...	4.3	58	0.27	9.1	16.2	95	4.9	8.8	6.06§	5.89	5.79§
May 31	.....	.....	.....	...	...	..	0.15	17.3	20.4	531	15.0	17.6	6.25	6.12	5.75

§ Uncontrolled.

TABLE 3.—DATA IN CASE 3*

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index †				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
May 4	184.5	.....	.....	0.32											
5- 6	180.0	530	2,905+	0.32	19.7+	65	0.27	6.7	16.5	73	9.5	23.3	6.40	6.10	5.92
6- 7	173.0	775	4,430	0.43	28.4										
7- 8	163.0	1,080	2,925	0.43	15.7	..	....	...	....	. .	6.7	19.0	6.46	6.02	6.06
8- 9	157 5	1,200	2,350	0.43	9.8										
9-10	153.5	1,200	2,524	0.43	8.4	..	....	...	....	...	3.0	8.8	6.35	5.84	6.13
10-11	150.5	1,200	2,135	0.43	8.4										
11-12	148.5	1,200	1,430	0.43	4.9										
12-13	146.5	1,200	1,720	0.43	3.9										
13-14	146.0	1,200	1,700	0.43	3.1										
14-15	144.0	1,500	1,390	0.43	2.1	42	0.45	3.5	11.4	13	1.3	4.2	6.24	5.75	6.11
15-16	143.5	1,200	1,520	0.60	2.0										
16-17	143.5	1,200	1,525	0.60	3.7										
17-18	143.5	1,200	1,620	0.60	1.8										
18-19	144.5	1,200	1,960	0.60	1.2										
19-20	143.5	1,200	1,705	0.60	1.2										
20-21	143.0	1,200	1,880	0.60	1.1										
21-22	142.5	1,200	1,150	0.60	0.6										
22-23	141.5	1,200	1,074+	0.40	lost	35	0.71	6.0	15.0	9	0.6	1 53	6.25	5.62+	6.25—
23-24	141.5	1,200	915	0.6	0.5										
24-25	142.0	1,200	1,580	0.6	0.6										
25-26	142.5	1,200	1,615	0.6	0.6										
26-27	141.5	1,200	1,500	0.6	0.9										
27-28	142.0	1,200	1,565	0.6	0.6										
28-29	140.3	1,200	1,940	0.6	1.0										
29-30	141.5	1,200	1,505	0.6	1.1										
30-31	139.7	1,200	1,310	0.6	1.3	42	0.25	4.3	10.9	45	0.9	2.1	6.13	5.62+	6.13—
31-June 1	140.5	1,200	970	0.6	1.1										
1- 2	140.5	1,200	1,100	3.6	1.5										
2- 3	141.5	1,200	870	3.6	1.3										
3- 4	142.0	1,400	965	3.6	2.7										
4- 5	142.5	1,200	1,360	3.6	3.3										
5- 6	142.5	1,200	1,200	3.6	4.3										
6- 7	141.5	1,200	1,350	3.6	4.8	41	0.19	4.4	18.5	133	2.2	9.2	6.15	5.83	5.94
7- 8	142.5	1,200	1,440	3.6	5.3										
8- 9	142.5	.....	1,060	3.6	5.3										
9-10	143.0	.....	1,305	3.6	3.0										
10-11	142.3	1,200	960	3.6	4.5										

* The diet for the period May 4 to May 15 contained 1,300 calories and a nitrogen content of 5 gm.; from May 16 to May 30, 2,000 calories and 5 gm. nitrogen; from May 31 to June 25, 2,500 calories and 6 gm. nitrogen; from June 26 the diet contained 2,500 calories and a nitrogen content of 12 gm.

† Weight for index = 72.7 kg.

TABLE 3.—DATA IN CASE 3*—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
June 11-12	142.0	1,200	970	3.6	5.4										
12-13	142.5	1,200	1,110	8.6	5.8										
13-14	143.5	1,200	1,215	8.6	9.7										
14-15	142.7	1,200	1,528	8.6	7.5	54	0.30	2.8	14.5	34	2.8	14.4	6.19§	5.90	5.91§
15-16	144.3	1,800	2,310	8.6	9.6										
16-17	143.5	1,800	2,010	8.6	9.6										
17-18	144.5	1,800	1,800	8.6	7.2										
18-19	144.5	1,760	1,357	8.6	7.3										
19-20	144.3	1,800	610	8.6	7.5										
20-21	144.7	1,800	1,150	8.6	8.7										
21-22	143.7	1,800	1,182	8.6	6.3	55	0.29	9.4	7.0	32	10.3	7.7	6.35	5.90	6.07
22-23	144.5	1,800	700	8.6	8.5										
23-24	144.7	1,800	795	8.6	12.2										
24-25	144.7	1,800	870	8.6	9.5										
25-26	144.7	1,800	1,990	8.8	17.9										
26-27	144.3	1,800	1,120	8.8	8.0										
27-28	144.0	1,800	1,180	8.8	10.0										
28-29	144.5	1,800	1,670	8.8	11.5										
29-30	144.0	1,800	1,620	8.8	11.2										
30-July 1	143.3	1,800	1,100	8.8	7.3										
1- 2	143.4	1,800	1,730	8.8	11.2										
2- 3	142.0	1,800	1,100	8.8	7.2	30	0.49	17.0	15.3	33	12.0	10.8	6.25	5.97	5.90
3- 4	140.0	1,800	1,705	4.8	8.1										
4- 5	.....	1,800	1,600	4.8	5.8										
5- 6	.....	1,800	1,480	4.8											
6- 7	.....	1,800	1,100	4.8	2.5										
7- 8	.....	1,800	1,550	4.8	2.3										
8- 9	.....	1,800	1,940	...	3.7										
9-10	.....	1,800	1,520	...	3.0										
10-11	.....	1,800													
11-12	.....	1,800	1,980												
12	.....	.....	.....	...	...	50	0.28	1.68	13.4	27	1.9	15.5	6.06§		
Jan.1,'18	....	.....	.....	...	...	..	0.20	2.0	14.9	65	2.1	15.6	6.60§	5.89	6.33

§ Uncontrolled.

TABLE 4.—DATA IN CASE 4

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sulphone-phthalein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Threshold
Feb. 19-20	102.0	2,000	1,840	2.0	3.3										
20-21	100.0	1,500	1,572	2.0	3.2	28	0.27	2.8	6.0	27	1.7	3.6	6.11	5.78	5.98
21-22	.....	1,500	1,000	2.0	4.0										
22-23	97.5	1,700	1,320	?	3.6										
23-24	.....	1,700	1,670	?	4.8										
24-25	95.0	1,700	1,710	?	3.4										
25-26	.....	1,800	1,060	3.0	1.7										
26-27	96.0	1,800	1,520	3.0	1.9										
27-28	.....	1,800	1,350	3.0	2.2										
28-Mar. 1	.....	1,800	1,330	3.1	2.4										
1- 2	94.5	1,800	1,600	3.1	3.2										
2- 3	94.0	1,800	1,692	3.1	3.5	37	0.67	7.0	15.2	19	2.2	4.8	5.92	5.81	5.73
3- 4	93.0	1,800	1,350	3.1	2.6										
4- 5	92.5	1,800	1,410	3.1	2.6										
5- 6	93.5	1,600	1,360	2.7	2.1										
6- 7	93.0	2,000	1,500	1.3	2.5										
7- 8	93.0	2,000	1,820	0.46	1.8										
8- 9	92.0	2,000	1,650	0.46	1.5										
9-10	90.5	1,600	1,720	0.45	1.2										
10-11	90.5	1,600	1,165	0.45	0.8										
11-12	90.5	1,600	1,440	0.26	1.4	21	0.71	7.2	6.8	7	0.7	0.6	6.03	5.62	6.02
12-13	89.5	1,600	1,179	0.2	0.7										
13-14	89.5	1,600	1,530	0.45	0.7										
14-15	89.0	1,600	1,260	0.46	0.8										
15-16	90.0	1,600	1,440	0.26	0.7										
16-17	89.0	1,600	1,950	0.26	4.3										
17-18	88.0	1,600	1,216	0.26	0.6	..	....	..	....	...	0.5	0.6	5.75	5.62	5.74
18-19	88.0	1,600	1,180	0.26	0.5										
19-20	88.0	1,600	910	0.46	0.4										
20-21	86.5	1,600	1,050	0.26	0.4										
21-22	86.5	1,480	1,010	0.22	0.5										
22-23	86.5	1,600	980	0.22	0.3										
23-24	86.0	1,600	1,060	0.22	0.4										
24-25	86.0	1,600	1,180	0.22	0.7										
25-26	86.0	1,600	850	0.22	0.3										
26-27	84.5	1,600	1,020	0.22	0.4										
27-28	85.0	1,600	987	0.22	0.4	15	0.96	8.2	7.6	5	0.5	0.4	5.75	5.62	5.74
28-29	86.0	1,600	1,220	0.643	0.3										

* Weight for index = 45.5 kg.

TABLE 4.—DATA IN CASE 4—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
March 29-30	80.0	1,600	1,500	2.14	0.5										
30-31	87.0	1,600	1,180	2.12	0.6										
31-Apr. 1	87.5	1,600	1,440	2.14	0.7										
1- 2	88.2	1,600	1,240	2.14	0.8										
2- 3	88.0	1,600	1,110	2.09	0.9										
3- 4	86.5	1,600	1,550	2.09	1.4										
4- 5	86.5	1,600	1,240	2.09	1.3										
5- 6	86.5	1,600	1,220	2.09	1.8										
6- 7	88.0	1,600	1,340	2.09	1.9	44	0.26	3.1	4.1	22	1.7	2.2	5.93	5.74	5.81
7- 8	87.0	1,600	1,360	2.09	2.0										
8- 9	87.0	1,600	1,130	2.00	1.7										
9-10	88.0	1,600	1,410	2.09	2.2										
10-11	88.5	1,600	1,550	2.09	2.2										
11-12	89.5	1,600	1,680	2.09	2.9										
12-13	89.0	1,600	1,170	2.09	2.0										
13-14	89.0	1,600	1,210	2.09	2.1										
14-15	90.0	1,600	1,350	2.09	1.9										
15-16	90.5	1,500	1,150	2.09	2.2										
16-17	88.0	1,600	1,300	2.09	2.4										
17-18	87.5	1,600	1,411	0.5	2.6	30	0.22	1.8	4.7	26	2.0	5.3	5.94	5.82	5.74
18-19	89.5	1,300	1,150	2.09	1.4										
19-20	89.0	1,760	1,327	2.09	2.6										
20-21	90.0	1,600	1,280	2.09	1.8										
21-22	89.5	1,600	1,700	2.09	2.0										
22-23	90.8	1,600	1,450	2.09	2.0										
23-24	91.0	1,500	1,610	2.09	2.7										
24-25	90.5	1,600	1,370	2.09	2.3										
25-26	92.0	1,600	1,210	2.09	2.5										
26-27	90.5	1,600	1,650	2.09	3.4										
27-28	89.5	1,600	750	2.09	1.6										
28-29	90.0	1,600	1,750	2.09	3.6										
29-30	89.5	1,400	1,370	2.09	3.9										
30-May 1	90.5	1,500	1,450	2.09	2.9										
1- 2	92.0	1,900	1,150	2.09	2.2										
2- 3	.....	1,300	1,150	2.09	2.5										
3- 4	89.5	1,600	956	2.09	2.6	37	0.16	2.6	4.6	58	2.0	3.5	6.09	5.78	5.84
4- 5	90.5	1,600	770	2.09	1.8										
5- 6	.....	1,500	1,270	2.09	2.6										

TABLE 4.—DATA IN CASE 4—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
May 6- 7	89.5	900	1,140	2.09	2.6										
7- 8	.....	1,000	1,330	2.09	2.9										
8- 9	91.0	900	1,110	2.09	2.5										
9-10	92.0	1,100	580	2.09	1.7										
10-11	92.0	1,100	850	2.09	1.7										
11-12	92.5	1,000	1,180	2.09	2.6										
12-13	92.5	1,300	1,140	2.09	2.9										
13-14	91.5	1,000	1,340	2.09	4.0										
14-15	92.0	1,000	1,150	2.09	2.5										
15-16	93.0	900	1,070	2.09	2.3										
16-17	92.0	1,100	961	2.09	2.2	42	0.18	2.3	4.2	50	3.0	3.3	5.93	5.79	5.75
17-18	92.5	1,000	1,230	2.09	2.8										
Nov. 12, 1917	.....	.....	.....	...	...	67	0.26	2.0	15.6	79					

TABLE 5.—Data in Case 5

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
May 15-16	139.0	1,200	292	...	0.3	15	1.41	11.9	4.0	1	1.2	0.4	6.59	5.62	6.58
16-17	138.5	1,065	735	0.5	0.7										
17-18	137.5	1,200	1,125	0.5	1.2										
18-19	134.5	1,200	810	0.5	0.9										
19-20	133.5	1,200	1,215	0.5	2.1										
20-21	129.0	1,200	1,505	0.5	3.0										
21-22	129.0	1,200	1,225	0.4	3.3										
22-23	128.5	1,200	1,520	0.4	4.3										
23-24	125.5	1,200	1,312	0.4											
24-25	123.5	1,200	1,460	0.4	5.3										
25-26	122.5	1,200	1,630	0.5	6.6	25	0.75	12.2	17.1	15	...	...	6.30		
26-27	122.5	1,200	1,180	0.76	4.0										
27-28	120.0	1,200	1,200	1.2	3.5										
28-29	121.0	1,200	1,080	1.2	3.1										
29-30	120.5	1,200	870	1.04	2.2										
30-31	120.0	1,200	365	1.04	1.4										
31-June 1	118.5	1,200	1,391	1.03	5.2	26	0.32	7.8	4.7	18	3.1	1.8	5.94	5.73	5.83
1- 2	118.0	1,200	1,650	1.03	5.0										
2- 3	116.0	1,200	1,880	1.03	6.4										
3- 4	115.5	1,200	1,620	1.03	5.2										
4- 5	112.5	1,200	1,660	1.03	3.2										
5- 6	111.5	1,200	1,900	1.03	6.1										
6- 7	109.0	1,200	1,900	1.03	2.9										
7- 8	108.0	1,200	1,860	1.03	4.8										
8- 9	108.0	1,200	1,250	1.03	4.4										
9-10	106.5	1,200	1,250	1.03	2.8										
10-11	105.3	1,200	1,650	1.03	4.6										
11-12	104.0	1,200	1,570	1.03	3.9	19	0.32	4.3	2.2	9	1.0	0.7	5.91	5.62	5.90

* Weight used for index = 68 kg.

TABLE 6.—Data in Case 6

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Feb. 26-27	123.5	1,500	690	0.37	1.6	20	1.56	6.8	3.9	0.5	1.1	0.6	6.13		
27-28	124.0	1,500	610	2.4	0.8										
28-Mar. 1	124.0	1,500	350 ?	2.4	0.8										
1- 2	123.5	1,500	544	2.4	0.5	..	....	...	....	...	0.9	0.4	6.19		
2- 3	123.5	1,500	730	0.52	0.7										
3- 4	125.0	1,500	440	0.28	0.3										
4- 5	.....	1,500	535	0.52	0.2										
5- 6	125.0	1,500	770	0.52	0.4										
6- 7	.....	1,360	350	0.52	0.1										
7- 8	125.5	1,500	400	0.52	0.2										
8- 9	126.5	1,500	630	0.52	0.2										
9-10	127.5	1,500	475	0.4	0.2	14	2.11	8.0	5.7	0.6	0.3	0.2	5.99		
10-11	127.0	1,500	630	0.52	0.2										
11-12	128.0	1,500	290	0.52	0.1										
12-13	128.8	1,500	355	0.5	0.1										
13-14	127.5	1,250	700	0.5	0.2										
14-15	131.0	1,500	355	0.5	0.1										
15-16	129.5	1,000	500	0.5	0.2										
16-17	127.5	1,000	600	0.5	0.2										
17-18	128.0	1,000	520	0.65	0.4										
18-19	128.5	2,000	640	2.5	0.2										
19-20	129.5	2,000	780	2.4	0.3										
20-21	130.5	1,710	490	1.9	0.1	6	2.15	7.7	3.7	0.4	0.3	0.2	5.38		
21-22	131.0	1,800	465	2.12	0.2										
22-23	130.0	1,790	680	2.50	0.2										
23-24	131.5	2,050	500	2.62	0.2										
24-25	131.0	2,000	766	2.40	0.2	..	....	...	....	...	0.3	...	5.20		
25-26	132.5	1,910	550	2.52	0.2										
26-27	136.5	2,000	620	2.52	0.2										
27-28	137.5	1,400	260	0.97	0.1	..	2.95	...	....	...	...	...	4.53†		
28-29	136.5	1,500	790	1.34	0.1										
29-30	136.0	1,800	750	2.04	0.1										
30-31	.....	1,750	775	1.76	0.1										
31-Apr. 1	137.0	1,850	680	2.15	0.1										
1- 2	.....	1,800	720	2.21	0.1										
2- 3	138.0	1,000	620	1.52	0.1										
3- 4	.....	1,750	810	2.48	0.2										
4- 5	.....	1,400	640	1.68	0.1										

* Weight used for index = 56.1 kg.
† NaCl in chest fluid = 4.88 gm. per liter.

TABLE 6.—DATA IN CASE 6—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
April 5- 6	140.0	1,925	490	2.45	0.1	..	3.30	...	....	...	...	...	4.45		
6- 7	.....	2,000	620	2.58	0.1										
7- 8	139.0	1,600	370	2.07	0.1										
8- 9	.....	1,500	630	2.48	0.3										
9-10	.....	1,250	430	1.43	0.1										
10-11	139.3	1,460	515	1.39	0.2										
11-12	138.0	1,225	420	0.39	0.2										
12-13	.....	1,500	370	0.25	1.1										
13-14	.....	1,425	410	0.49	0.2										
14-15	138.5	1,330	250+	0.40	0.1										
15-16	.....	440	240	0.40	0.1										
16-17	.....	1,100	260	0.40	0.2	..	4.36	4.5	0.4	...	...	...	4.56		
17-18	.....	1,100	230	0.40	0.2										
18-19	.....	675	170	0.30	0.1										
19-20	.....	1,000	100	0.40	0.1										
20-21	.....	.....	325	...	0.30	..	4.59	...	....	...	...	...	4.45‡		

‡ April 21. Tissue juices at operation 4.69 gm. per liter of NaCl.

TABLE 7.—DATA IN CASE 7

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Dec. 4- 5	157.0	1,000	400	...	2.6										
5- 6	.....	1,900	1,100	3.0	5.1	58	0.19	5.6	19.0	155	2.3	7.9	6.26	5.82	6.06
6- 7	.....	1,500	1,820	3.0	10.6										
7- 8	152.0	2,000	2,540	3.0	11.2										
8- 9	148.9	2,000	1,700	3.0	7.9										
9-10	146.7	2,000	2,050	3.0	6.4										
10-11	.....	2,000	2,500	3.0	8.0										
11-12	143.4	2,000	1,760	1.0	5.4										
12-13	143.2	2,000	1,620	1.0	3.2										
13-14	143.0	2,000	1,645	1.0	3.3	..	0.14	3.0	12.3	135					
14-15	142.3	2,000	2,200	1.0	4.0										
15-16	141.7	2,000	2,000	1.0	4.7										
16-17	141.9	2,000	1,705	1.0	4.6										
17-18	.....	2,000	1,710	1.0	4.1										
18-19	141.9	2,000	2,000	1.0	4.7										
19-20	141.7	2,000	1,540	1.0	2.4										
20-21	.....	2,000	1,356	1.0	2.4	44	0.13	1.9	4.8	52	2.6	6.7	6.31	5.81	6.22
21-22	144.8	2,000	1,406	1.0	3.4										
22-23	143.0	2,000	950	1.0	2.0										
23-24	143.2	2,000	1,240	1.0	1.4										
24-25	.....	2,000	1,260	1.0	0.9										
25-26	.....	2,000	1,720	1.0	1.3										
26-27	144.9	2,000	1,240	1.0	1.5										
27-28	146.3	2,000	1,755	1.0	3.0										
28-29	148.1	2,000	1,500	1.0	2.0										
29-30	148.1	2,000	1,120	1.0	1.5										
30-31	149.6	2,000	1,300	1.0	1.6										
31-Jan. 1	....	2,000	1,300	1.0	2.0										
1- 2	.....	1,600	1,440	1.0	1.8										
2- 3	151.4	2,000	1,170	1.0	1.2										
3- 4	.....	2,000	1,708	1.0	3.0	40	0.24	3.5	9.5	39	2.1	5.7	6.45	5.78	6.29
4- 5	152 9	2,000	1,020	6.0	2.9										
5- 6	150.5	600	910	6.0	6.2										
6- 7	151.8	970	750	6.0	5.8										
7- 8	151.8	1,200	755	6.0	6.0										
8- 9	155.3	2,000	890	6.0	3.8										
9-10	155.3	2,000	1,050	6.0	3.2										
10-11	155.3	2,000	1,545	6.0	4.1										
11-12	155.3	2,000	870	6.0	3.4										

* Weight used for index = 71.8 kg.

TABLE 7.—DATA IN CASE 7—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Jan. 12-13	155.9	2,000	1,110	6.0	5.5										
13-14	157.9	2,000	1,500	1.8	7.8										
14-15	.....	1,200	1,960	1.0	5.2										
15-16	152.4	800	1,040	0.0	4.3										
16-17	.....	1,050	675	1.2	0.2										
17-18	.....	1,200	445	1.3	0.2										
18-19	151.1	1,450	813	1.5	0.4	71	0.14	10.0	19.0	200	0.9	0.9	5.98	5.62	5.97
19-20	.....	1,500	1,160	1.5	0.5										
20-21	153.1	1,680	1,165	1.2	0.5										
21-22	.....	1,450	910	1.8	0.5										
22-23	154.2	1,430	690	1.9	0.3										
23-24	.....	1,200	740	1.2	0.4										
24-25	.....	850	360	1.0	0.2										
25-26	.....	1,600	510	1.6	0.2										
26-27	154.0	1,400	760	1.6	0.2										
27-28	153.3	1,200	620	1.6	0.2										
28-29	.....	1,200	820	1.6	0.2										
29-30	153.1	1,200	640	1.6	0.2										
30-31	152.6	1,200	660	1.0	0.2										
31-Feb. 1	153.1	1,200	1,200	1.0	0.3										
1- 2	152.2	1,200	720	1.0	0.6										
2- 3	.....	1,200	840	1.0	1.1										
3- 4	152.7	1,200	775	1.0	1.1	48	0.12	2.7	6.9	97	1.1	2.8	6.08	5.72	5.97
4- 5	.....	1,200	810	1.0	0.8										
5- 6	152.7	1,200	740	1.0	1.5										
6- 7	.....	1,200	1,210	1.0	1.7										
7- 8	153.3	1,200	660	1.0	1.3										
8- 9	154.0	1,200	615	1.0	0.7										
9-10	153.6	1,200	1,000	1.0	1.7										
10-11	153.6	1,200	950	1.0	3.7										
11-12	.....	1,200	1,000	1.0	5.9										
12-13	.....	1,200	960	1.0	3.7										
13-14	151.5	1,200	1,310	1.0	3.7	55	0.14	2.2	6.3	59	2.0	5.9	6.00	5.79	5.82
14-15	150.0	1,200	1,600	1.0	6.0										
15-16	147.5	1,200	1,330	1.0	5.1										
16-17	147.5	1,200	1,860	1.0	7.2										
17-18	145.0	1,200	1,340	1.0											
18-19	143.5	1,200	470	1.0	1.6										

TABLE 7.—Data in Case 7—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Feb. 19-20	142.0	1,200	300	1.0	0.6										
20-21	141.5	1,200	250	1.0	0.2										
21-22	141.5	1,200	481	1.0	0.2	34	0.26	9.1	6.1	34	0.4	0.3	5.96		
22-23	142.5	1,200	560	1.0	0.2										
23-24	142.5	1,200	790	1.0	0.2										
24-25	142.5	1,200	660	1.0	0.3										
25-26	142.5	1,200	650	1.0	0.4										
26-27	142.0	400	340	1.0	0.5										
27-28	141.0	1,200	260	1.0	0.5										
28-Mar. 1	139.5	1,200	240	0.8	0.4										
1- 2	140.0	1,500	330	1.6	0.3										
2- 3	142.0	1,400	370	2.0	0.3										
3- 4	142.0	1,500	560	1.6	0.3										
4- 5	142.5	1,200	880	1.6	0.2										
5- 6	142.5	1,200	710	1.6	0.2										
6- 7	142.5	1,200	712	1.6	0.3	45	0.37	8.7	14.8	40	0.5	0.8	6.13		
7- 8	142.5	1,200	580	1.6	1.3										
8- 9	142.5	1,200	970	1.6	5.1										
9-10	143.2	1,200	492	1.8	0.5	..	....	...	....	...	1.7	0.5	6.36		
10-11	144.3	1,200	510	1.7	0.7										
11-12	145.0	1,400	610	1.8	0.6										
12-13	145.5	1,200	470	1.7	0.4										
13-14	146.5	1,200	530	1.8	0.5										
14-15	146.5	1,200	680	1.6	1.3										
15-16	146.0	1,200	520	1.4	0.6										
16-17	147.0	1,200	710	1.8	1.0										
17-18	148.3	1,200	840	1.8	0.7										
18-19	149.0	1,200	550	1.8	2.0										
19-20	148.7	1,200	710	1.8	2.6										
20-21	148.0	1,200	662	1.8	0.8	50	0.36	8.9	12.1	35	1.3	1.7	6.09		
21-22	150.0	1,200	510	1.8	0.5										
22-23	150.5	1,200	700	1.8	3.0										
23-24	152.5	1,200	600	1.5	1.6										
24-25	152.5	1,200	480	1.2	1.1										
25-26	152.5	1,200	360	1.5	1.0										
26-27	.....	1,200	700	1.5	1.8										
27-28	152.0	1,200	1,310	1.9	2.2										
28-29	151.0	1,200	750	1.9	2.6										

TABLE 7.—DATA IN CASE 7—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
March 29-30	151.5	1,200	710	1.4	3.4										
30-31	150.5	1,200	800	1.1	3.7										
30-Apr. 1	.....	1,200	900	1.1	5.2										
1- 2	149.0	1,200	930	1.2	4.6										
2- 3	147.5	1,200	920	0.9	5.4										
3- 4	146.0	1,200	1,650	0.8	5.3	55	0.21	3.5	10.3	55	3.1	9.0	5.89	5.85	5.66
4- 5	144.0	1,200	1,900	0.8	8.3										
5- 6	142.0	1,200	1,100	1.3	2.9										
6- 7	140.0	1,200	1,000	1.3	3.6										
7- 8	139.0	1,200	1,430	1.6	4.1										
8- 9	138.5	1,200	1,050	1.6	2.7										
9-10	138.5	1,200	1,000	1.6	3.0										
10-11	138.5	1,200	900	1.6	1.8										
11-12	139.0	1,200	760	1.6	1.3										
12-13	140.0	1,400	600	1.8	1.3										
13-14	141.0	1,350	1,020	1.7	1.3										
14-15	141.5	1,350	994	1.9	1.4	24	0.17‖	2.3‖	6.6‖	43‖	0.8	2.3	6.03		
15-16	140.5	1,350	590	1.8	1.2										
16-17	142.0	1,350	720	...	1.5										
17-18	142.5	1,350	1,220	1.0	3.7										
18-19	141.0	1,350	1,120	1.0	1.1										
19-20	141.5	1,350	1,390	1.0	1.3	..	0.39	5.7	22.2	43	0.7	2.8	6.00		
20-21	141.0	1,350	1,120	1.0	0.7										
21-22	142.5	1,350	1,380	1.0	0.7										
22-23	140.5	1,350	1,450	1.0	2.3										
23-24	140.5	1,350	910	1.0	0.6										
24-25	.....	1,350	1,450	1.0	0.5										
25-26	140.0	1,350	1,720	1.0	1.1										
26-27	140.0	1,350	1,290	1.0	1.8										
27-28	139.0	1,400	1,401	8.0	3.5	40	0.28	5.9	21.1	81	1.9	6.7	5.94	5.79	5.77†
											3.6	3.9	6.24	5.78	6.08‡
28-29	.....	1,350	1,078	1.0	3.3						3.8	5.2	6.34	5.70	6.16¶
											3.5	4.1	6.33	5.78	6.17#
29-30	140.0	1,350	1,380	0.9	2.9						4.1	4.8	6.16	5.80	5.98**
30-May 1	130.0	1,350	1,830	1.0	5.0										
1- 2	137.5	1,350	1,650	1.0	5.3										
2- 3	137.0	1,760	1,432	1.0	1.6										
3- 4	137.0	1,350	1,180	1.0	0.8										
4- 5	136.7	1,350	950	1.0											

† At 9 a. m.; 3.5 gm. NaCl at 12 n.; 3.5 gm. NaCl at 1 p. m.
‡ At 1 p. m. April 27.
¶ At 3 p. m. April 27.
# At 5 p. m. April 27.
** At 12 n. April 28.
‖ Results uncontrolled.

TABLE 7.—DATA IN CASE 7—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
May 5- 6	135.5	1,350	1,080	1.0	0.8										
6- 7	.....	1,350	830	1.0	0.5										
7- 8	136.5	1,350	730	1.0	0.4										
8- 9	136.5	1,350	730	4.0	0.4										
9-10	137.5	1,360	720	4.0	0.6										
10-11	138.0	1,350	840	4.0	0.4										
11-12	139.5	1,350	700	4.0	1.0										
12-13	140.5	1,350	1,380	4.0	6.2										
13-14	141.0	1,350	715	4.0	2.1										
14-15	141.0	1,350	770	4.0	2.1										
15-16	142.0	1,350	1,236	4.0	2.3	52	0.34	8.8	21.8	70	1.5	3.7	6.24	5.74	6.12
16-17	143.0	1,350	870	4.0	2.4										
17-18	143.5	1,350	1,140	0.9	2.2										
18-19	143.5	1,350	1,360	0.8	1.2										
19-20	143.0	1,350	960	...	0.9										
20-21	.....	.....	815	...	0.7										
21-22	.....	.....	1,240	...	0.4										
1917 June 26	.....	.....	.....	...	...	50	0.28	3.1	15.3	43	2.2	10.8	6.29	5.85	6.06
Nov. 28	.....	.....	.....	...	...	65	0.21	2.4	18.0	79	2.1	15.8	6.50	5.89	6.23

TABLE 8.—Data in Case 8

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sulphone-phthalein	Urea Index				Chlorid Index *				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Threshold
Dec. 4- 5	.....	880	1,073	...	0.7	20	1.25	14.9	20.4	8	0.3	0.4	0.41§		
5- 6	166.3	1,800	1,140	2.4	0.5										
6- 7	165.0	1,800	1,140	2.4	0.6										
7- 8	163.5	1,800	1,060	2.4	0.9										
8- 9	163.5	1,800	1,240	2.4	1.7										
9-10	162.1	1,800	1,115	2.4	1.1										
10-11	.....	1,800	1,100	2.4	1.1										
11-12	161.3	1,800	1,000	2.4	1.2										
12-13	161.7	1,500	920	1.1	1.3										
13-14	160.4	1,500	1,060	1.1	1.5										
14-15	159.7	1,500	950	1.1	1.7										
15-16	159.3	1,500	950	1.1	1.8										
16-17	159.0	1,500	995	1.1	1.7										
17-18	.....	1,500	840	1.1	1.9										
18-19	158.6	1,500	640+	1.1	2.0										
19-20	158.4	1,500	870	1.1	2.0										
20-21	159.1	1,500	768	1.1	1.5										
21-22	158.8	1,500	790	1.1	1.9										
22-23	.....	1,500	830	1.1	1.9										
23-24	159.0	1,500	1,180	1.1	2.5										
24-25	.....	1,315	1,560	1.1	4.4										
25-26	160.0	1,500	1,125	1.1	2.4										
26-27	157.0	1,535	1,600	1.1	1.9										
27-28	.....	1,500	1,275	1.1	2.0										
28-29	155.0	1,500	1,600	1.1	2.0										
29-30	155.0	1,500	1,225	1.1	2.2										
30-31	156.0	1,500	1,300	1.1	1.8										
31-Jan. 1	155.5	1,500	1,375	1.1	2.8										
1- 2	155.5	1,500	1,250	1.1	3.0										
2- 3	155.5	1,460	1,300	1.1	2.2										
3- 4	154.5	1,500	1,700	1.1	3.1										
4- 5	154.5	1,500	1,410	1.1	3.3										
5- 6	153.5	1,500	1,230	1.4	1.3										
6- 7	153.5	1,500	1,600	1.4	4.8										
7- 8	152.0	1,500	1,740	1.4	3.5										
8- 9	151.5	1,500	1,480	1.4	3.4										
9-10	149.5	1,500	1,360	1.4	2.7										

* Weight used for Index = 58 kg.
§ Uncontrolled.

TABLE 8.—DATA IN CASE 8—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Jan. 10-11	150.0	1,500	1,500	1.4	3.5										
11-12	149.5	1,500	1,400	1.4	3.1										
12-13	149.5	1,500	2,050	1.4	4.8										
13-14	148.5	1,500	1,400	1.4	3.7										
14-15	149.0	1,500	1,650	1.4	4.0										
15-16	147.5	1,500	1,540	1.4	4.1	5	0.39	5.2	1.9	5					
16-17	147.0	1,500	1,500	1.4	4.2										
17-18	146.5	1,500	1,500	1.4	4.2										
18-19	146.5	1,500	1,460	1.4	4.0										
19-20	146.0	1,500	1,180	1.4	3.4										
20-21	145.0	1,500	1,600	1.4	4.5										
21-22	143.5	1,500	1,540	1.4	4.5										
22-23	144.0	1,500	1,400	1.4	4.2										
23-24	142.5	1,500	1,500	1.4	5.6										
24-25	141.7	1,500	1,600	1.4	6.5										
25-26	141.3	1,500	780	1.4	2.5										
26-27	140.0	1,500	480+	1.4	1.5	15	0.22	4.1	7.3	47	3.2	5.8	6.31	5.83	6.11
27-28	142.0	1,500	2,000	1.4	6.0										
28-29	141.0	1,500	1,350	1.4	7.2										
29-30	140.0	1,500	2,260	1.4	8.8										
30-31	138.0	1,500	2,760	1.4	8.3										
31-Feb. 1	135.5	1,500	2,020	1.4	5.7										
1- 2	134.0	1,500	2,500	1.4	7.0										
2- 3	132.5	1,500	2,017	1.4	4.3	16	0.28	2.7	10.3	40					
3- 4	130.5	1,500	1,880	2.0	7.6										
4- 5	131.5	1,500	1,940	2.0	5.0										
5- 6	.....	1,500	2,800	2.0	7.5										
6- 7	127.5	1,500	2,470	1.7	8.4										
7- 8	125.0	1,500	2,210	1.7	7.6										
8- 9	123.5	1,500	2,380	1.8	7.8										
9-10	121.0	1,500	2,180	1.7	7.4										
10-11	120.3	1,500	2,290	1.7	7.3										
11-12	118.0	1,500	2,450	1.7	8.2										
12-13	116.5	1,500	2,810	1.8	8.8										
13-14	115.3	1,500	2,510	1.8	8.4										
14-15	113.0	1,500	2,255	1.8	8.4	25	0.38	4.9	10.5	25	4.3	9.3	6.26	5.90	5.98
15-16	111.0	?	2,310	1.8	8.2										

TABLE 8.—DATA IN CASE 8—(*Continued*)

Date	Weight, Lbs.	Fluid Exchange		Chlorid Exchange		Phenol-sul-phone-phthal-ein	Urea Index				Chlorid Index				
		In	Out	In	Out		Blood Urea	C	D	Index	C	D	Plasma NaCl	Calcul. Plasma NaCl	Thresh-old
Feb. 16-17	109.5	1,500	2,020	1.8	5.9										
17-18	107.5	1,500	1,980	1.8											
18-19	.....	1,500	1,580	2.1	3.5										
19-20	107.5	1,500	1,220	2.3	1.0										
20-21	106.7	1,500	1,670	1.8	1.3										
21-22	108.5	1,500	1,600	1.8	0.9										
22-23	108.8	1,500	1,550	1.8	0.9										
23-24	109.0	1,500	1,628	1.8	1.1	17	0.59	5.7	8.7	9	1.4	2.1	5.88	5.72	5.78
24-25	107.0	1,500	1,380	1.8	1.4										
25-26	109.5	1,500	1,560	1.8	1.2										
26-27	108.3	1,500	1,460	1.8	0.6										
27-28	109.0	1,500	1,600	1.8	0.6										
28-Mar. 1	110.5	1,500	2,000	1.8	0.6										
1- 2	109.5	1,500	1,760	1.8	0.6										
2- 3	109.1	1,500	1,645	1.7	1.0										
3- 4	108.5	1,500	1,490	1.7	0.8										
4- 5	.....	1,500	1,520	1.8	0.8										
5- 6	111.0	1,500	2,132	1.4	0.8	21	0.61	7.1	17.1	19	0.6	1.3	6.33		
6- 7	110.5	1,500	1,790	1.7	0.9										
7- 8	114.5	1,760	1,677	11.7	2.1	..	....	...	....	...	0.7	1.0	6.48†		
8- 9	114.5	1,500	2,060	1.8	2.7						0.6	0.7	6.50‡		
9-10	115.0	1,500	2,080	1.8	3.4										
10-11	112.5	1,500	1,910	1.8	3.2										
11-12	113.5	1,500	1,940	1.8	2.4										
12-13	113.8	1,500	1,780	1.8	1.6										
13-14	114.0	1,500	2,060	1.8	1.8										
14-15	113.5	1,500	1,490	1.8	1.6										
15-16	113.5	1,500	1,595	1.7	1.6										
16-17	114.5	1,500	1,840	1.7	1.2										
17-18	114.5	1,500	2,080	1.7	1.5										
18-19	113.0	1,500	1,780	1.8	1.5										
19-20	.....	400	830	0.0	1.4										
20-21	.....	1,625	1,820	2.4	2.2										
21-22	.....	2,115	1,950	2.1	4.2										
22-23	111.5	2,280	2,200	2.9	3.1										
23-24	113.0	2,155	1,680	2.2	2.3										
24-25	111.5	2,200	2,029	1.7	1.5	21	0.37	8.0	8.5	27	1.5	1.6	6.35	5.72	6.27
1917 May 1	.....	.....	.....	...	...	38	0.20	3.4	4.4	31	5.9	7.9	6.50	5.90	6.22

† At 10 a. m.
‡ At 11 a. m.; 10 gm. NaCl at 10:30 a. m.

had a large diuresis were uniformly emaciated. The final urine examination showed albuminuria in every case but Case 2, although red blood cells persisted in only one case (4). Case 2 was accepted for the National Army in August, 1917, and the man sailed for France in January, 1918, apparently well. Cases 3 and 4, after about a year, are in perfect health and have resumed their previous work without difficulty. In Case 5 the man reports, after seven months, that he is too well to return for observation. In Case 1 the woman reports that she is sick in bed in another city. Case 8 says that he feels better than ever before in his life, although he still has hypertension and albuminuria. Case 7 had a long period of persistent edema, weakness and dyspnea, but when last seen, over a year after her admission, had no edema and was symptomatically very much improved. In brief, the final results show clinical recovery in three out of six acute cases, reported freedom from symptoms in one, and unknown illness after practical recovery in one. Neither chronic case made a clear-cut recovery, although they are both symptomatically well at present.

DISCUSSION OF FUNCTIONAL FINDINGS

The phenolsulphonephthalein test, the renal test day, the blood urea and urea index were used in the functional studies. A renal test day was done on five cases (Table 1), in each case during the last of the hospital stay and during a period of water balance as evidenced by a constant weight. The balances of salt and nitrogen, so frequently included in the performance of this test, were omitted because of the obvious unreliability of a twenty-four-hour experiment. Moreover, in view of its great dependence on a factor so variable as the amount of water excreted, systematic determinations of the specific gravity over a brief period must be very carefully interpreted. There was nocturnal polyuria in all the cases, most marked in Case 2, which in every way was the mildest. The night specific gravity was below 1.019 in all except Case 7, in which it was 1.022. The variation of specific gravity during the test day was consistently normal except in Cases 1 and 4. But since this variation is worth little more than its highest figure, indicative of the concentrating ability, we can say that every case except Case 4 showed in some specimen during its course a normal power of concentration, 1.020 or above; in fact, one of the chronic cases concentrated more highly than is seen in the average normal specimen. Of the two cases (1 and 4) showing "maximal impairment" of the test as a whole according to Mosenthal, Case 1 did not have a subnormal renal function at any time during the period of observation, and Case 4 made a complete recovery, reaching a concentration of 1.028 some months later. It seems clear that in acute nephritis, the renal test day is of no great value; it may, indeed, be quite misleading.

The phenolsulphonephthalein excretion of the series covered a range of figures from 0 to 79 per cent., varying considerably in the individual cases and often far from consistent with the clinical and laboratory findings. If, however, only gross changes are considered, they assume a certain significance. The admission phenolsulphonephthalein was 20 per cent. or less in the three most severe cases (5, 6 and 8), but in the other five, varying from 26 per cent. to 65 per cent., there is little relation between the picture implied by the first phenolsulphonephthalein excretion and that found to be true by longer study. For example, Cases 1 and 2, in every way the least severe, show excretions of 28 and 44 per cent., respectively, while Cases 3 and 7 with far more persistent disease, excreted 65 and 58 per cent. But in all the cases subsequent observations fit in more satisfactorily with the rest of the picture, so that it is possible to say that the average phenolsulphonephthalein excretion gives a fair idea of the severity of the dis-

TABLE 9.—DATA OF TESTS IN AUTHOR'S CASES

Case	Night Total	Night Sp. Gr.	Variation Sp. Gr.	Total Output	Weight Balance	Time in Course	Function at Time
1	765	1.013	1.008-1.010	2,220	0	Late	Normal
2	1,315	1.015	1.011-1.028	1,913	sl. neg.	Late	Normal
3	505	1.019	1.010-1.030	1,357	0	Late	Normal
4	612	1.010	1.008-1.012	1,554	0	Late	Phth. normal Ambard 30
5	.....	.....	1.023-1.012*				
6	.....	.....	1.022-1.019*				
7	604	1.022	1.016-1.026	1,352	0	Late	Normal
8	.....	.....	1.014-1.026*				

* Variation during observation in hospital; no test day given.

ease. These cases suggest that in acute nephritis variations above a level of 20 to 25 per cent. are rarely of real functional significance, although one may add that a figure below 20 per cent. is of rather more serious import, not of the immediate outcome but of the degree of involvement as demonstrated by other methods of study. Yet it is necessary to note the complete recovery of the patient, Case 4, who excreted on one occasion only 15 per cent. of phenolsulphonephthalein.

Urea retention was found on admission in only three cases (5, 6 and 8), most marked in the fatal case, but above 1.2 gm. per liter in each. Three of the other cases (1, 2 and 7) showed no elevation during their entire period of observation, but the remaining two patients (Cases 3 and 4) presented an unusual picture. On a low nitrogen and salt diet they retained urea steadily, reaching in the first instance a crest of 0.71 gm. in two and a half weeks, and in the second a crest of 0.96 gm. in five weeks. These figures decreased gradually and were normal on the patients' discharge in spite of increased nitrogen in the

diet. To summarize the acute cases, the highest figure for blood urea was in the only fatal case, the other high figure was undoubtedly the next most severe and the two cases without any evidence of poor urea function were the most favorable; the blood urea estimations, therefore, have provided the most consistently valuable means of determining the degree of the process in any given case. Even here we cannot avoid noting that the chronic case, in which recovery was most delayed, showed at no time a retention of urea.

A study of the laws of urea excretion as formulated by Ambard and confirmed by McLean pictures to the reader physiologic laws so definite that they can be mathematically expressed, variables so few that they can be included in a small formula, a formula that will give exact expression of the ability of the kidney to excrete urea. On determining a number of indexes and observing the wide discrepancies found in the same person, normal or pathologic, the inclination is strong to discard the formula entirely. Further determinations, however, demonstrate that the basal laws may be applied in a very general way, and that the index, if interpreted liberally, may often contribute something of value to the diagnosis, although isolated determinations may lead far afield. In other words, as the expression of a physiologic law, the urea index is quite untenable, as are its fundamental formulae, but as a rough clinical test of one aspect of renal function, it has a place. This slight value is due to the fact that a pathologic kidney so frequently retains urea and is unable either to concentrate normally or to excrete the usual amount of urea, all factors tending to decrease renal function as expressed by the index. If we overlook variations above the normal and consider the usual rather than the average figures during a period of observation, we have in the urea index an expression of the general renal function that fits fairly well with the impression gleaned from other data. The two mildest cases (1 and 2) of our series were always normal or above, Cases 3 and 4, somewhat more severe, were more frequently below normal, while Case 6, with fatal outcome, presented the greatest impairment. Of the chronic cases, one finds in Case 7, nine out of seventeen indexes below normal, within variations from 34 to 200; and in Case 8, consistently low results throughout. In only one case (5) was there constant agreement between the Ambard and the phenolsulphonephthalein, but in the majority there were striking discrepancies; for example, in comparing the figures of Case 1 on admission and discharge, we see that the Ambard drops from 235 to 75, while the phenolsulphonephthalein rises from 38 to 64 per cent., and in Cases 2 and 3, with practically constant phenolsulphonephthalein excretions, the urea index goes from 70 to 118, in one, and from 9 to 133 in the other. But the fact remains that the average gross function expressed by the two tests agrees within the limits of clinical necessity, for forty-two subnormal Ambards were

accompanied by thirty-five subnormal phenolsulphonephthaleins; this in sixty-two observations. (Assuming phenolsulphonephthalein 50 per cent. and Ambard 70 as normal limits.) But I would hasten to say that even moderately rigid interpretation of the Ambard as a real index of the degree of impairment of urea function may lead to the greatest error. This criticism of the Ambard is based on such observations as the following. In Case 2 at constant levels of blood urea, an increased water excretion caused a 28 per cent. decrease in the index, although the rate of excretion (D) was the same, February 28, volume of urine, 94 c.c.; blood urea, 0.38 gm.; rate D, 22.5 gm.; index, 98; March 14, volume of urine, 204 c.c.; blood urea, 0.37 gm.; rate D, 22.4; index 70, while in Case 3 the apparent function was higher when the kidney excreted at the rate of 7 gm. than when it excreted 13 gm. June 21, the blood urea was 0.29 gm., urine concentration 9.4 gm., rate D 7.0 gm., index 32, and on July 12 the blood urea was 0.28 gm., urine concentration 1.7 gm., rate D 13.4 gm., index 27.

Four observations under constant conditions on Case 4 with rates of excretion varying less than 0.5 gm. showed indexes from 22 to 50 due mainly to small fluctuations in the blood urea. Case 8 had a rate of 2 gm. during a period when the blood urea was decreasing and a rate of 10 gm. during retention, although the blood figures at the two observations were the same.

While the wide variations of the urea index are not always accompanied by comparable changes in renal function as judged by other means, yet these results have a certain scientific interest. The most striking observation in the series is the fact that there was in every case a drop in the index during clinical improvement. In Case 1 a decrease from 235 to 75 unaccompanied by any other evidence of functional change has only an exceptionally low blood urea (0.1 gm. per liter) in the first observation to explain the higher figure. Two months after the lower figure (75) was found, another determination was made and with an unchanged blood urea a 40 per cent. increase in the water output raised the index to 111. Case 2 immediately after diuresis fell from 98 to 70, although the blood urea and total excretion (D) were constant. One month later, the extraordinary figure of 531 was obtained, notwithstanding the fact that the rate of excretion was practically the same as that of the other six observations; explicitly it was 20 gm. as compared with an average of 19 gm. on previous determinations ranging from 16 to 22 gm. There were too few observations on Case 5 to permit satisfactory discussion of his results, but here again there is a drop from 18 to 9 after diuresis, although the patient continued to improve. While these three cases are similar in a lowered urea index after marked clinical improvement, there is in no case an accompanying change in the other tests of renal function, in particular, no urea retention; and in Cases 1 and 2 the

changes are seemingly due to the vagaries of the formula. There is, however, quite a different picture in Cases 3 and 4, in which the falling Ambard is paralleled by a retention of urea and a moderate decrease in the phenolsulphonephthalein excretion. Case 3 during a remarkable diuresis, losing 38 pounds in nine days, went from 0.27 to 0.45 gm. per liter, and after coming into balance eight days later the figure was 0.71 gm. During this time the index dropped from 65 to 9, although the rate of output (D) was the same for both observations. Meanwhile, the nitrogen intake was constant and there was no change in the patient's general condition. Case 4 lost very little weight, but the blood urea increased steadily from 0.27 to 0.96 gm. per liter in a period of five weeks, while her index dropped from 28 to 5. Her nitrogen intake was decreased from 10 gm. to 5 gm. one week after the first sign of retention. In both cases the urea fell from its highest figures to normal in about ten days, with a coincident rise in the Ambard and phenolsulphonephthalein but with no other observed changes. It is important to point out the absolute clinical unsimilarity of these two cases. There was no significant abnormality of salt function accompanying this phenomenon.

This puzzling urea retention while the patient is recovering may be due to a general impairment of renal function, or, overlooking the rather inconsistent phenolsulphonephthalein variations, to some change in the urea mechanism. Mason's[5] suggestion that the first normal figures are due to a stimulated function requires the rather difficult assumption that the process, the nature of which is unknown, markedly impairs the renal function for water and salt, while at the same time it stimulates the urea function. Moreover, since every case but one (Case 1) in this series returned to a function at least as high as the original one, under "stimulation," it seems more probable that the original figure was merely a fairly normal one, while the "slump" was due to some factor occurring in the course of the disease. It is obvious that the retention is too much delayed to be a phenomenon of blood concentration. An increased blood urea may be due to an unusual presentation of urea to the body; here we have two factors to be considered, the low caloric diets forcing use of body protein and the considerable wasting during diuresis. But both these factors were present in Case 2, while in Case 4 an early decrease of 5 gm. in the nitrogen intake did not influence the course. The other obvious manner of increasing the blood urea is by a lowered power of excretion. There may have been renal fatigue due to the large excretion of water or salt, but the striking diuresis in Case 2 was not thus effective. Since we know nothing of the nature of this disease, or diseases, we can, of course, suggest that this curious functional change may be part of its

5. Mason: THE ARCHIVES INT. MED., 1918, **21**, 261.

natural course. The most convincing argument that a decreased urea function was not instrumental is the picture in Case 4. Here we have an increase of blood urea in a rate of excretion (D) of 6 to 15 gm., and a decrease on a constant excretion of 4 gm. (four observations), over a period of six weeks; in other words, during retention the kidney was excreting urea much better than when there was the opposite reaction. What difference can it make that the kidney was working under the stimulus of a greater blood urea when it was excreting at the higher rate? If the kidney could take care of a certain intake of nitrogen with a rate of 4 gm., it should certainly do so with a rate of 15 gm. The writer realizes that the essential weakness of this argument is that his rate (D) is calculated from an isolated two hour observation, as is Ambard's index, but the consistent difference between the two sets of figures may lessen the weight of this criticism. Where, then, may we seek an explanation of this retention if we cannot find an increased production of urea or a definite decrease in the ability of the kidney to excrete it. If we decline to consider the kidney a fixed and unchanging valve in the bottom of a cylinder of blood, and remember that it is of the same fundamental substances and subject to the same laws that apply to blood, then we cannot be so exacting in our demand for a mathematical relationship between the blood urea and urine urea. Since this organ of excretion is itself so largely composed of blood, it seems obvious that its function cannot be expressed by a constant but will depend on the physico-chemical changes that may occur in the blood. There may, therefore, be shifts in the constituents of the blood that will not be mirrored by the urine. In Case 6 a rising blood urea is accompanied by a fall in the plasma chlorid to the extremely low level of 4.45 gm. per liter, although there had been complete retention of chlorids for a period of some weeks. This change may be due to a shift in other blood constituents, and was probably necessary to preserve the osmotic relations. We have discussed this "recovery retention" at greater length than our material deserves, because it seems to point to variables not recognized by our present formulae of urea excretion.

It is interesting to consider the widely varying urea indexes found in these patients in view of McLean's[6] suggestion that fixation of the index is a sign of moderate renal impairment. Case 7, for instance, with chronic renal disease, varied from 34 to 200; others varied even more strikingly.

DISCUSSION OF SALT AND WATER EXCHANGE

Edema was present in every case. In two cases, 1 and 4, it had so greatly diminished before admission that there was no striking diuresis under observation. These patients lost a little weight and swept out

6. McLean: Jour. Exper. Med., 1917, **26**, 181.

small quantities of salt, but they came very quickly into equilibrium and remained so. Case 6 was never able to excrete salt or water and his edema steadily increased until death. There was in Case 5 a continued loss of weight amounting to 35½ pounds for the month of observation, and the patient's salt and water balances were consistently negative. Two cases, however, showed a remarkable diuresis; Case 2 lost 30 pounds, and Case 3, 41 pounds in eleven days, the daily losses reaching as high as 10 pounds. The decreasing edema was accompanied by a great sweeping out of salt and water, but after reaching a constant weight neither patient showed any abnormality of salt or water function in the daily balances.

The sequence of events in diuresis was possible of study in Case 2 and in certain periods of Case 7, one of the chronic cases who had alternate periods of increasing and decreasing edema. It seems clear that the salt function is the first to be regained, followed at varying intervals by the pouring out of water with a coincident decrease in weight. Case 2 was excreting comparatively little water the first day of admission, but had already begun to put out large quantities of salt; the next day the water elimination more than doubled with a quite disproportionate increase in salt excretion. Events moved so rapidly here that a close analysis is impossible, but in Case 7, at one period the salt excretion began steadily to increase ten days before the increase in water excretion or the drop in weight was evident. This relationship of the salt excretion to diuresis is confirmatory of other known facts that point to a very close relationship between chlorid function and edema. Another feature of the mechanism demonstrated by Case 2 is the fact that the water loss by urine and stool during diuresis covers a surprisingly low percentage of the weight loss for the period. Over two periods, one entirely accurate and the other practically so, this case had daily water loss of 1,110 c.c., and 1,285 c.c., respectively, to be accounted for by vaporization. This is a definite increase above normal and demonstrates that the skin and lungs may assume a large share in the excess excretion of water. It is interesting to note that the amount of chlorids that should theoretically be excreted, were the weight lost a solution with the concentration of the blood, agrees fairly well with actual salt loss. In Case 2, over a seven day period the theoretical figures for a 12.7 kg. loss of weight would be 76 gm., and actual loss was 63 gm. Case 3 in seven days lost 76 gm. compared with a calculated 78 gm., and in Case 5 for twenty-five days it was 94 gm. theoretical, 74 gm. actual. Of course, these balances are not entirely accurate, for the chlorids of stools and sweat were not estimated. Nevertheless, they are sufficiently close to suggest that there is no storing of chlorids in concentrations above that of the blood. Four of the cases were given varying amounts of added salt during convalescence and in no case was there gain in weight or failure to

handle the extra intake, which was 3.3 gm. in Case 1, 4.6 gm. in Case 2, 8.8 gm. in Case 3, and 2 gm. in Case 4. It may be added that the course in Case 3 seemed to point out that over 8 gm. was too much to be given safely in these cases. Both of the chronic cases gained weight when salt was administered, and it is worth noting that in salt function only did their findings differ characteristically from the acute cases.

The concentration of chlorids in the plasma was generally at its highest point on admission and decreased during diuresis in every instance; the greatest drop was 0.65 gm. per liter in Case 5, and the most rapid drop was in Case 2, in which it fell 0.35 gm. in three days. Although the association of a high concentration with marked edema is apparently another result confirming the causative rôle of chlorids in this abnormal accumulation of fluid, it must be noted that three of the cases returning without edema after a period of ordinary diet had high figures, so it is possible that the low chlorid diet under treatment accounts for this drop after admission. The plasma chlorid was always lower during a salt poor diet, increasing with the addition of more salt, but the variations thus caused were relatively small; the greatest increase was only 0.23 gm. per liter in Case 3, after several days of 8.8 gm. of salt a day. One of the most interesting observations was the marked fall in concentration in Case 6 (from 6.19 to 4.45 gm. per liter) over a period of practical suppression of urinary chlorid excretion. Subcutaneous edema fluid, uncontaminated by blood, obtained at operation, showed the same low figure, as did also the chest fluid; we may, therefore, assume a fairly general fall in body fluids. There was a coincident increase in edema, but it was not sufficient to charge the change in concentration to dilution of the blood, as the following calculation will show. At a concentration of 5 gm. to the liter, an increase in weight of 7.7 kg. would require 38.5 gm. of salt to bring its concentration to that of the blood, whereas the amount of salt given up by 56 kilograms of body fluids (70 per cent. of the body weight) in a drop of 1.67 gm. per liter, would be 66 gm., and there was, moreover, a positive balance, intake and urine output, of practically 50 gm. It is clear, therefore, that we may have a gradually increasing total salt content in the body with a diminishing concentration in the plasma not due to dilution by fluid retention. We are forced to consider it a shift due to changes in the physico-chemical environment. At least two possibilities are suggested by this case; one is the forcing of the chlorids into the corpuscles by change in the carbonate concentration, the Zunst[7] reaction; or, an increase in other blood constituents, such as the high blood urea, may demand a readjustment to preserve the osmotic balance. In any case, we have

7. Zunst: Beitr. z. Physiol. d. Blutes., Bonn, 1868.

the illuminating fact that there may be a very great change in the plasma chlorid concentration independent of intake or urinary excretion, and paradoxical to the apparent chlorid balance.

In no case was the rate of excretion clearly dependent on the concentration of chlorids in the plasma. In general, the latter tended to remain quite constant when equilibrium was established after diuresis, while the urinary output was proportional to the daily intake of salt. With identical plasma chlorids the rate of excretion showed the widest variation under different dietary régimes. For example, Case 2, with with a constant plasma concentration, excreted at a rate of 0.6 gm. on a salt poor diet, and at 13.6 gm. when 4 gm. of salt were added daily to the intake; Case 3 with 6.13 gm. per liter in the blood excreted 2.2 gm. on a very low intake, while seven days later with an increased intake his excretion was 9.2 gm. and the plasma 6.15 gm. per liter; Cases 1 and 4 show the same relation to a lesser degree. It would be difficult to ascribe these variations to changes in the course of the disease. If the rate of excretion is so independent of the plasma concentration, it is evident that the threshold according to McLean's formula could be greatly changed by the ingestion of salt. As a matter of fact, we find it changing in Case 2 from 5.84 on a salt poor diet to 5.58 on an intake of 4 gm. a day, and similarly in Case 3 from 6.25 to 5.9. The reaction to a single administration of 7 gm. of salt is interesting. It is most clear cut in Case 2, in which there is a rise in plasma concentration of about 0.2 gm. with no change in excretion, although forty-eight hours later, with the same plasma chlorid, the rate of excretion has increased seven times. Obviously, some other factor than the concentration of chlorids in the plasma was responsible for the increased excretion.

The fundamental theory of the chlorid index requires only the foregoing data to demonstrate its physiologic impossibility. We have published elsewhere[8] even more conclusive evidence of the effect of dietary modification on the chlorid threshold in normal individuals. But the clinical value is quite aside from the accuracy of the formula, and if we find a fairly consistent relationship between the threshold and the severity of the disease, we may consider the test of value. As a matter of fact, while the threshold is elevated in almost every case and is highest in the severest case, practically every high threshold depends on one of two factors, a low excretion due to a very low intake, or a plasma concentration considerably higher than normal. Of course, this increased concentration may be caused by a raised threshold, but Case 6 with a threshold of 6.1 at admission decreased his concentration to an extraordinary extent, although the urinary

8. Atchley: Proc. Soc. Exper. Biol. and Med., 1918, **15**, 85.

excretion showed no evidences of increased renal permeability to salt. Since any threshold determined during a salt-poor régime is entirely misleading, the frequency of this régime in nephritis makes the clinical application of the chlorid index rather limited. This much is clear; there is no definite constant threshold for any individual, nor is the height of the threshold an index of the degree of impairment of chlorid function. More valuable than what the formula expresses are the facts that may be gathered from a determination of the plasma chlorid concentration, together with a knowledge of the daily intake and output of salt. There are fairly conclusive grounds for saying that an abnormally high plasma chlorid on a moderate salt intake may be the only evidence of a latent disturbance of chlorid metabolism.

THERAPY

Since the fundamental principles that underlie this disease are still a mystery, all attempts at therapy must take the most general lines. There is fortunately one brilliant exception in the relation of sodium chlorid to edema; a relationship long known if little understood. The first step in the treatment of acute nephritis is, therefore, restriction of the sodium chlorid intake. Beyond this move, the general principles suggested by this study may be briefly recounted, remembering always that each case is a distinctive picture and will require distinctive treatment. The caloric requirement of the patient should be maintained from the very beginning, in as palatable a form as is possible, and after diuresis has occurred he should be moderately overfed. Empirically, it is wise to give a low protein intake in all cases of acute nephritis, the degree of restriction depending largely on the amount of urea in the blood. To be more explicit, when there is no retention of urea, 8 or 10 gm. of nitrogen is a safe intake, but if there is an abnormal figure, 6 gm. should be the upper limit. The latter amount should not be exceeded if gross hematuria is present. Theoretically, the urea index should give us the most valuable information about the ability of the kidney to handle nitrogenous foods, but the facts presented demonstrate its unreliability for that purpose. (Case 3 was increasing his blood urea with an index of 25, while Case 5 was decreasing his at an index of 15). While a limited (1,200 c.c.) fluid intake is the method of choice, fluids may be forced (2,500 c.c.) with benefit in certain stubborn cases, particularly if there be nitrogen retention. The patient should be confined to bed until diuresis is complete, as evidenced by a week of fairly constant weight, although gross hematuria is always a contraindication to being out of bed. One cannot escape the conclusion that our therapy here is merely an attempt to prevent traumata that would interfere with nature's readjustment of forces unknown at present.

GENERAL SUMMARY

Any attempt to classify this series on an anatomical basis would of necessity be entirely speculative and will, therefore, be omitted. Moreover, until there is some definite knowledge of the physiologic anatomy of the kidney, the cataloguing of clinical pictures by anatomic names seems to be unjustified and confusing. If there be hematuria we can say that there probably is some degree of acute inflammation and treat the case accordingly. But beyond that a diagnosis such as glomerulo-nephritis is incomplete, perhaps unfounded, and does not contribute in any way to the treatment of the case. The duration of the pathologic process previous to the appearance of symptoms is another point quite impossible to determine, and if it were possible to guess fairly accurately, little of value would be contributed thereby. Case 7, for instance, is called chronic merely because albuminuria was accidentally discovered some years before the present attack, which otherwise was of an acute onset fairly similar to those of the true acute cases.

These patients are grouped together because they became acutely ill with the constant presence of edema, albuminuria and hypertension, findings of so-called renal origin. A closer analysis of the indivdual cases proves each to be a separate and distinct picture. It is quite impossible to subdivide them further without omitting one or more essential points of difference. One is also unable to predict the course or outcome from the original picture on admission. Prognosis is, therefore, very unsatisfactory. Every case is an individual problem and only by means of a careful study over a moderately long period of time can its status be determined. This study should confine itself to the scope of our knowlegde of the pathologic physiology of renal function. First of all, the salt function determined by the concentration of chlorids in the plasma, together with the daily chlorid balance; second, the water balance discovered by frequent weighings and observation of the fluid exchange; and last, the urea function as demonstrated by the height of the blood urea on a known nitrogen intake. Other factors such as hematuria, anemia, or hypertension are, of course, important, but secondarily so. In treating diabetes we are satisfied, clinically, with its simple terminology and proceed to investigate the peculiarities of the disease in a particular individual. In like manner, it would seem logical to call the type of case described in this paper an acute renal syndrome and investigate the variations in function peculiar to each case without demanding that every variation be added to the terminology of the diagnosis.

In conclusion, one must express the feeling that the investigation of this disease has been hindered by an interest too closely restricted to the kidneys. A broader study of the chemical balances of the body as a whole may demonstrate that the kidney is of secondary importance.

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